A DISSERTATION ON

# PT AND APTT AS AN EARLY MARKER IN ASSESSMENT OF HEMATOTOXIC SNAKE BITE AS COMPARED TO WHOLE BLOOD CLOTTING TIME IN A TERTIARY CARE HOSPITAL COIMBATORE-641018.

Submitted to

**THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY**
**CHENNAI – 600032**

In partial fulfilment of the Regulations
for the Award of the Degree of

**M.D. BRANCH - I**
**GENERAL MEDICINE**


**DEPARTMENT OF GENERAL MEDICINE**

**COIMBATORE MEDICAL COLLEGE HOSPITAL**

**COIMBATORE-641018**

**MAY 2019**

# DECLARATION

I solemnly declare that this dissertation entitled **"PT and aPTT as an early marker in assessment of hematotoxic snake bite as compared to whole blood clotting time"** bonafide and genuine research work carried out by me at Coimbatore Medical College and Hospital, from (Feb 2017 to Feb 2018), during the academic year 2016-2019, under the guidance and supervision of **Dr. SWAMINATHAN, MD.,** Professor, Department of Medicine, Coimbatore Medical College Hospital, Coimbatore.

This dissertation is submitted to the Tamil Nadu Dr.M.G.R. Medical University, towards the partial fulfilment of requirement for the award of M.D.Degree in General Medicine (Branch-I).

Place: Coimbatore **Dr. MHASISIELIE ZUMU**

Date:

# CERTIFICATE I

*Certified that this is the bonafide dissertation done by* ***Dr. MHASISIELIE ZUMU*** *from Feb 2017 to Feb 2018 during the academic year 2016 to 2018 and submitted in partial fulfillment of the requirements for the Degree of* ***M.D.,General Medicine****, Branch I of* ***The Tamil Nadu Dr. M.G.R. Medical University, Chennai.***

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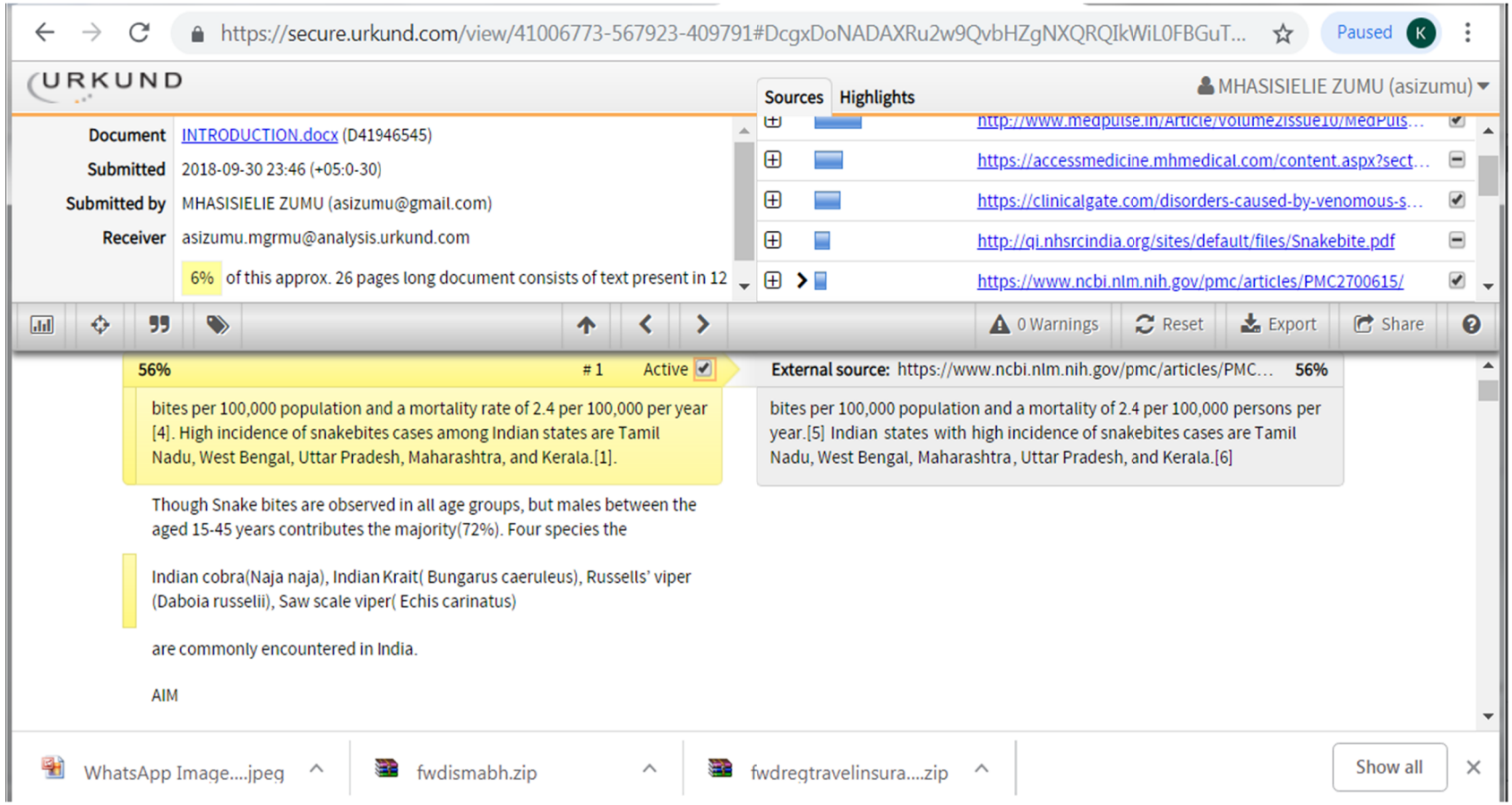
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bites per 100,000 population and a mortality rate of 2.4 per 100,000 per year [4]. High incidence of snakebites cases among Indian states are Tamil Nadu, West Bengal, Uttar Pradesh, Maharashtra, and Kerala.[1].
Though Snake bites are observed in all age groups, but males between the aged 15-45 years contributes the majority(72%). Four species the
Indian cobra(Naja naja), Indian Krait( Bungarus caeruleus), Russells' viper (Daboia russelii), Saw scale viper( Echis carinatus)
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bites per 100,000 population and a mortality of 2.4 per 100,000 persons per year.[5] Indian states with high incidence of snakebites cases are Tamil Nadu, West Bengal, Maharashtra, Uttar Pradesh, and Kerala.[6]
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**Dr. MHASISIELIE ZUMU**

# ABBREVIATIONS

| | | | |
|---|---|---|---|
| 1. | ASV | - | Anti-Snake Venom |
| 2. | ADR | - | Adverse Drug Reactions |
| 3. | ADE | - | Adverse Drug Event |
| 4. | AKI | - | Acute Kidney Injury |
| 5. | WHO | - | World Health Organization |
| 6. | AChE | - | Acetylcholinesterase |
| 7. | GSI | - | Geographical Survey of India |
| 8. | CPR | - | Cardio Pulmonary Resuscitation |
| 9. | WBCT | - | Whole Blood Clotting Count |
| 10. | aPTT | - | Activated Prothrombin Thromboplastin Time |
| 11. | PT | - | Prothrombin Time |
| 12. | RBC | - | Red Blood Cells |
| 13. | ABG | - | Arterial Blood Gas |
| 14. | DIC | - | Disseminated Intravascular Coagulation |
| 15. | ATIII | - | Antithrombin III |
| 16. | WBCT | - | Whole Blood Clotting Time |
| 17. | IM | - | Intramuscular |
| 18. | IV | - | Intravenous |
| 19. | M | - | Male |
| 20. | F | - | Female |
| 21. | D | - | Day |
| 22. | N | - | Night |
| 23. | SHTN | - | Systemic Hypertension |
| 24. | DM | - | Diabetes Mellitus |

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# INTRODUCTION

Snake bite is of significant health concern, especially in rural areas of tropical and subtropical countries. Snake bite is common amongst farmers, plantation workers, construction workers, snake charmers, hunters, snake rescuers, and migrant populations in tropical and subtropical countries. Urbanization and deforestation has made snake bite an important public health problem. In India, snake bite takes a lot of human lives, and therefore warrant urgent attention. High mortality is due to poor rural health services and delay in initiating anti snake venom. About 49 000 people in India die every year of snake-bite[31], although the figure is probably under-rated because most rural Indian population consults a traditional healers and so goes unreported. And also Doctors at primary health centres in India have less experience in, management of snake bites. Many victims die on the journey to tertiary hospitals. WHO's inclusion of snake-bite envenoming in the list of category A as neglected tropical diseases in early 2009[28]. It has been reported that in up to 80% of snake bite cases in developing countries, first attend a traditional healers before consulting a medical centre ***[2,3].*** Maharashtra has reported an incidence of 70 snake bites per 100,000 population and a mortality rate of 2.4 per 100,000 per year ***[4].*** High incidence of snakebites cases among Indian states are Tamil Nadu, West Bengal, Uttar Pradesh, Maharashtra, and Kerala.[1]**.** Though Snake bites are observed in all age groups, but males between the aged 15-45 years contributes the majority(72%). Four species the Indian cobra(Naja naja),

Indian Krait( Bungarus caeruleus), Russells' viper (Daboia russelii), Saw scale viper( Echis carinatus) are commonly encountered in India.

# AIM AND OBJECTIVES

## AIM

This study mainly focuses on the PT and aPTT as an early marker for detection of snake bite, hematotoxicity as compared to Whole blood clotting time

## OBJECTIVES

1. PT and aPTT as an early marker for detection of snake bite, hemotoxici ty as compared to Whole blood clotting time .
2. Early administration of anti snake venom can avoid hemotoxic compli cations, excess loading of anti snake venom and anti snake venom com plications.

# REVIEW OF LITERATURE

Snake bite poisoning is known to man since antiquity.

All snakes are predatory carnivores. Since snakes are preyed upon by other animals they tend to be secretive and have evolved many survival strategies. Many species are mainly nocturnal (night hunters) e.g. kraits, but other species are mainly diurnal (day understanding about the habits of snakes, simple precautions can be adopted to reduce the incidence of snake bites. About 2500-3000 species of snakes exist in the world. Most venomous snakes are found in Asia as compared to the other area of the world, 250 species and subspecies, out of which 50 are poisonous. In India, out of the 216 species of snakes, 60 are considered poisonous[36]. The families of poisonous snakes include Elapidae, Viperidae and Hydrophidae which are responsible for neurotoxicity, vasculotoxicity and myotoxicity respectively. Viperidae family includes two subfamilies: Viperinae (classic vipers) and Crotalinae (pit vipers). Elapidae family includes cobras and common kraits. Hydrophidae are the sea snakes Viper bites are more common than the other venomous snake bites in human beings. Viper bites are responsible for vasculotoxicity leading to bleeding tendencies and coagulation defects. These bleeding diatheses are mostly caused by consumptive coagulopathy, anti coagulation, fibrinolytic or may be due to direct effect of snake venom on platelet aggregation. Early detection of vasculotoxicity and prompt institution of anti venom therapy can prevent serious complications due to snake envenoming. Presence of coagulopathy is the

absolute indication for anti-venom administration, which is the specific treatment of snake bite.

Case Fatality due to snake bite can be attributed to a wide species variation, shortage of anti-snake venom(ASV), poor treatment protocols, lack of public education and lack of proper trained health professionals. It is estimated that there are over 1,000,000 snakebites in India alone leading to between 45 000 and 50 000 deaths annually[51] . Reliance on traditional healers and false believe further compound the problem. High death rate cannot be attributed to superstition and lack of awareness only, as there are a number of victims who die after seeking medical treatment, the reason being lack of experience health provider and non-compliance with the existing treatment protocol. Snake bite is a medical emergency, where timely intervention can reduce both morbidity and mortality. Lack of knowledge about simple measures of prevention, occupational hazard and inappropriate first-aid measures all magnify the problem. Difficulty in accessibility to health care services, difficulty in transportation and subsequent delay in Anti Snake Venom administration result in high mortality. The time since snake bite is of vital importance, because with time more venom gets bound to the tissues, making it less manageable for neutralization by Anti Snake Venom. Further, use of Anti Snake Venom may be avoided due to inexperience and fear of anaphylaxis or irrationally use of ASV when not indicated, resulting in total wastage of resources and also exposing the patient to toxicity risk. There is also lot of uncertainty in the dosage of Anti Snake Venom, though National Protocol on Snake Bite Management formulated by the

MOHFW(Ministry of Health & Family Welfare, Government of India) is in place besides the WHO Guidelines[33,34].

Hematotoxic abnormalities are the most common manifestation of snake envenoming global. Most of the viperid, and some elapid, venoms activate common pathways of coagulation resulting in consumptive coagulopathy. Snake Venom induced coagulopathy is brought about by activation of the clotting pathway by procoagulant toxins, resulting in clotting factor consumption and coagulopathy. The type of procoagulant toxin differs between snakes and can activate prothrombin, factor V, and factor X or consume fibrinogen. Fibrinogen, which is the common final substrate of the coagulation cascade, is invariably low in this condition. However, fibrinogen assay is not generally available, especially in remote areas where snakebites are prevalent. Therefore, alternative blood tests are required for initial evaluation, follow-ups and monitoring responses after antivenom therapy in snakebite victims.

A simple 20-min whole-blood clotting test (20WBCT) has been shown to correlate with fibrinogen levels in patients bitten by Bothrops sp. in South America[30]. Consequently, the WHO recommended this method for evaluation of coagulopathy in snakebite patients. In addition, a standard Lee and White venous clotting time (VCT), in conjunction with platelet counts, was shown to be predictive for systemic bleeding in a multivariate analysis of green pit viper bitten patients. While these tests are relatively rapid and simple, their accuracy has rarely been evaluated. Furthermore, they are usually performed at the bedside by personnel not well trained in laboratory medicine and, therefore,

they are subject to error. Training of the treatment team is critical for the reliability of these tests.

PT(Prothrombin time) and aPTT(activated partial thromboplastin time) are better standardised tests with well-established quality control systems. They are available in many hospitals and can be automated, thus assuring their precision. In addition, the international normalized ratio (INR) values harmonise PT tests performed in different laboratories using different commercial reagents. However, data on their uses in viper bitten patients are lacking. We hypothesised that PT and APTT would be effective for the assessment of viper bitten patients.

Delayed administration of ASV in case of hematotoxic snake bite can lead to complication of consumptive coagulopathy, acute renal failure, excess administration of anti snake venom , complications of anti snake venom administration, fresh frozen plasma transfusion and death .

While snake bite is observed in all ages, the large majority are in males between the age of 15-45 years. The predominance of male victims suggests a special risk of outdoor works.

**SPECIES**

There are some 2700 described species of snakes in the world coming under 402 genera and 18 families, of these some 500 species are venomous. 275 species of snakes have been described from India belonging to 71 genera and 11 families. Out of these 275 species 62 species can be cate-

gorized as ‘Venomous’ 42 as ‘mildly venomous’ and 171 as ‘non venomous’. Of the 62 venomous species, 42 are seen on land and 20 in the sea.

**In India the poisonous snakes belong to three broad families.**

Family –Elapidae – (Cobras, Kraits & Coral Snakes)

Family –Viperidae –The family of Viperidae has two subfamilies , Viperidae (Rus sell’s Viper, Saw Scaled Viper) and Crotalinae (Pit Viper)

Family – Hydrophidae –Sea Snakes

**In India, ‘Four’ among the poisonous snakes are highly venomous.**

1. Cobra–Najanaja(Spectacled,Cobra),
2. Russell’sViper-(Daboiarusselli )
3. Saw Scaled Viper (EchisCarinatus),
4. Krait (BungarusCaerules)

Other deadly snakes may be going unnoticed and causing death and disability. The recent discovery of the Hump nosed Pit Viper (Hypnale Hypnale) as a species capable of causing life threatening symptoms

In order to determine the actual list of medically significant species in India, the old concept of “The Big 4” is to be abandoned for a newer more flexible model that enables better classification of species. In the Indian setting, almost two-thirds of bites are attributed to saw-scaled viper (as high as 95% in some areas like Jammu and Kashmir) , about one fourth to Russell's viper and smaller proportions to cobra and kraits. In Sri Lanka, Daboia russellii accounts for 40% of bites and Naja naja for another 35% · Daboia russelliialone

accounts for 70% bites in Myanmar. However, clinical features and outcomes are not as simple to predict because every bite does not result in complete envenomation.

## IDENTIFICATION

## POISONOUS OR NON-POISONOUS SNAKES

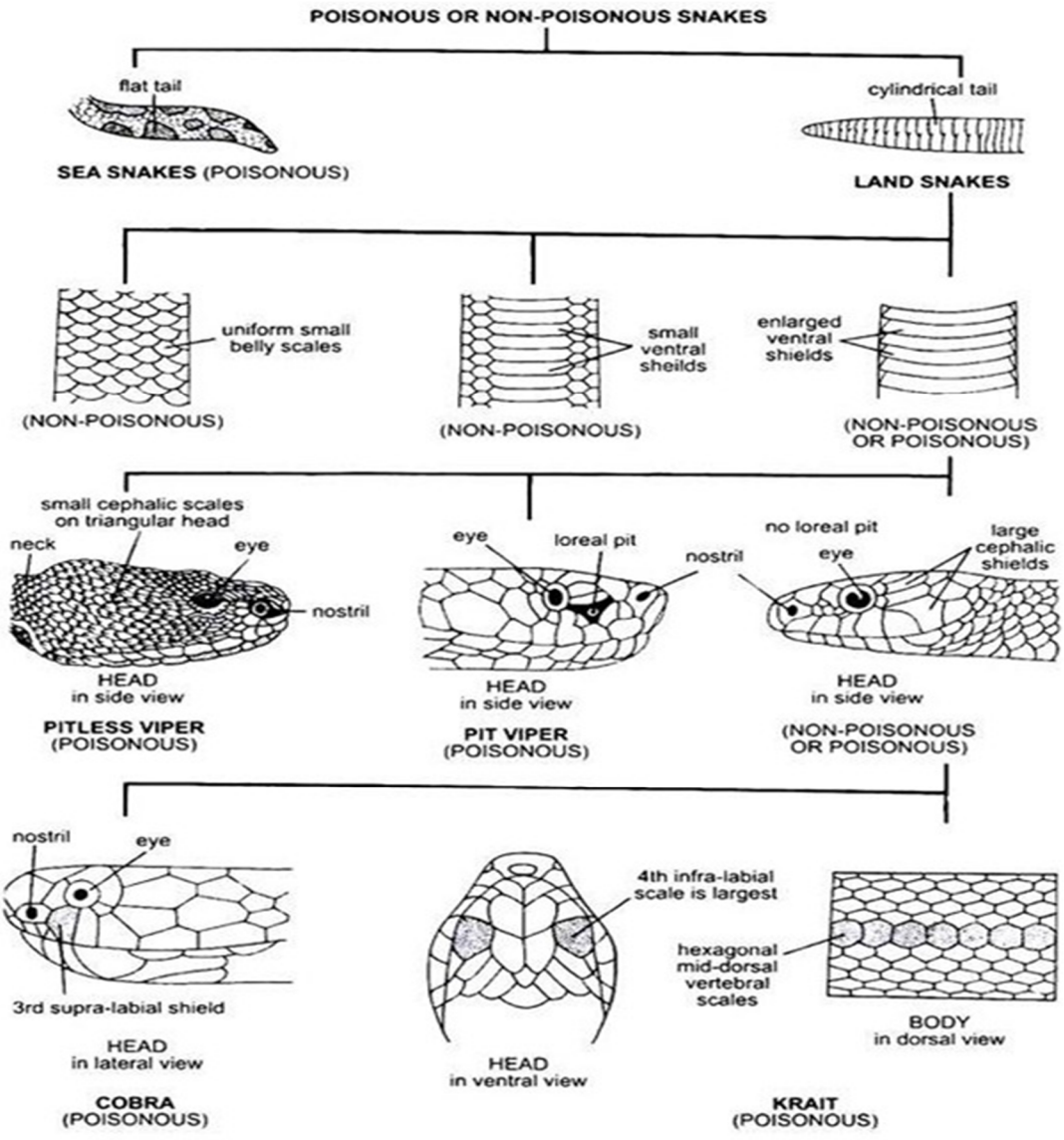



**Fig. 23.5.** Diagram for identification of poisonous and non-poisonous snakes.

**Fig : 1**

## Identification of Snake species

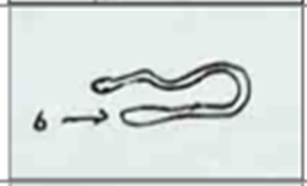
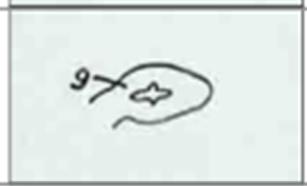
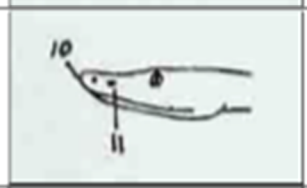
| | | |
|---|---|---|
| Black snake, vertebrals (1) larger than costals (2). Fourth infralabial (3) large. |   | Kraits. Highly venomous. *Bungarus caeruleus* & *Bungarus ceylonicus* |
| Distinct hood with two constant ventral spots (4) and variable dorsal markings (5). |   | Cobra. Highly venomous. *Naja naja*. |
| Flat, rudder-like tail (6). |   | Seasnakes. Venomous. Family HYDROPHIIDAE |
| Head triangular (7) with "V" mark. Three rows of spots (8) along the body. |   | Russell's viper. Highly venomous. *Daboia russelii*. |
| Small snake with cross mark on the head (9). |   | Saw-scaled viper. Venomous. *Echis carinatus*. |
| Small snake, head triangular, snout raised (10). A pit between the snout and nostril (11). |   | Hump-nosed pit vipers. Venomous. *Hypnale* spp. |
| Stout, large green snake. Head triangular. A pit (12) between the eye and the nostril. |   | Green-pit viper. Venomous. *Trimeresurus trigonocephalus*. |
| Large, thick snake. Head triangular with labial pits (13). Quadrangular markings on the body (14). |   | Python. Dangerous. *Python molurus*. |

**Fig : 2**

## INDIVIDUAL SPECIES IDENTIFICATION:

## SAW SCALED VIPER

*Scientific Name*

*Echis carinatus.*

*Other Common Names*

Carpet viper; “Phoorsa”.

*Geographical Distribution*

All over India (especially plains and deserts).

*Physical Appearance*

1. Saw-scaled viper grows upto 1½ to 2 feet long, they are usually brown in colour, with a wavy white line across the entire length of each flank, a diamond-shaped markings over the back, usually numbering 25 to 30.
2. Triangular head with small scales. Whitish color arrow-shaped mark is often present on the head with pupils vertical in shape.
3. Saw-scaled viper is named so because its serrated scales. When agitated, the snake throws itself into a double coil (“figure of eight”), and rubs the coils together vigorously. At the same time by exhaling forcefully through the nostrils producing a loud hisse.
4. Saw-Scaled viper is viviparous.
5. It is an aggressive snake. Slightest provocation can cause the snake to bite.

*Habitat*

This snake prefers desert regions, and is often found basking in the sun during the daytime, among rocks or in sandy soil. It may enter human habitations especially tents, in search of prey. In some parts of peninsular India, it is very uncommon, particularly in most parts of Kerala.

*Nature of Venom*

Vasculo- and haemotoxic. 0.0046 gram of venom is injected at the time of bite.

**Fig 3 : Saw Scale viper**

## RUSSELL'S VIPER:

This snake got its name from a Scottish herpetologist Patrick Russell who was the first person to describe many Indian snakes. Daboia is derived from Hindi word which translates for "that lies hid".

*Scientific Name:-*

*Vipera russelli, Daboia russelli.*

*Geographical Distribution:-*

All over India.

*Physical Appearance*

1. It is a brownish, stout snake and grows up to several feet in length.
2. The snake has a triangular head, with a 'V' shaped mark (apex forward pointing), which are covered with small scales and has vertical pupil.
3. Fangs of the snake are long, channelised, and hinged .
4. The snake has 3 rows of chained dark spots over the entire body. It is known to hiss loudly when agitated. It is viviparous.
5. They are nocturnal snake, but during the daytime, it often rests up under bushes, base of trees or in leaf litter.

*Nature of Venom*

Predominantly vasculo- and haemotoxic, but also can produce neuro-toxic effects . The snake has also been associated with Acute renal failure and adrenal insufficiency. At the time of bite it injects 63 mg of venom .


**Fig 4 : Russell's Viper**

## COMMON KRAIT:

*Scientifi c Name:-*

*Bungarus caeruleus.*

*Other Common Names:-*

Indian krait.

*Geographical Distribution:-*

All over India.

*Physical Appearance*

1. The snake is steel-blue in colour and can grow up to 3 to 4 feet in length, with whitish bands brown in colour.
2. They have a small dark eyes with almost invisible pupils. The upper lip is yellow or white in colour and the belly is very white.
3. A chain of hexagonal large scales is seen throughout the mid doral aspect of the body. The ventral scales are undivided distal to the vent, unlike other elapids. The fourth infralabial scale is the largest of the infralabial.

*Habitat*

The common krait is a reclusive snake which prefers to reside in crevices of rocks or logs of wood, and being nocturnal, emerges only during the night to hunt for prey. Its primary diet is other snakes. It can be found all over Peninsular India and often seeks habitation near human dwellings.

The common krait may enter houses and hide in dark corners, cupboards, bookshelves, etc. It does not hiss, but occasionally makes a faint whis-

tling sound. These snakes prowl on hot humid nights; they often do not strike, but make a quick snapping bite.

*Nature of Venom*

Predominantly neurotoxic. It is the most venomous snake of India.


**Fig 5 : Common Krait**

## INDIAN COBRA :

*Scientific Name:-*

*Naja naja.*

*Other Common Names:-*

Indian Cobra.

*Geographical Distribution*

All over India.

*Physical Appearance*

1) It is usually brown or black in colour.
2) It can grow up to 5 to 6 feet in length. The neck is distensible that can be expanded into a hood. Dorsal side of the hood, there may be a monocellate or binocellate mark. It has alternate wide and narrow, transverse, dark bands. Dorsal hood is mark by a pale circle edged with black and has 1 to 3 spots; ventral hood mark has a pair of dark spots, or a wide dark band.
3) The hood markings is the hallmark of cobra, and its habit of rearing up when alarmed.
4) Ventral surface of the hood are faint, broad, black stripes above which are two dark spots that extend over 3 to 4 scales.
5) The head of the snake is small, and pupils are round.
6) The 3rd supralabial shield touches the eye and nose shield.

*Habitat*

Grassy plains, fields, and mountainous regions (up to 15000 feet). They usually reside among piles of bricks, termite mounds, tangles of roots at the base of trees, and old masonry constructions. The spectacled cobra is encountered virtually over the whole of mainland India except the north-east. The black cobra (*Naja oxiana*) occurs in the extreme north of India around Jammu and Kashmir, and also in Gujarat and Rajasthan, although these may be patternless versions of the spectacled cobra. The cobra is diurnal, but bites from cobras occur during both the day and the night. The cobra's principal diet is rats. It is known to enter human habitations in search of prey.

*Nature of Venom*

Cobra venom is cardio toxic, neurotoxic, haematotoxic and cytotoxic. Predominantly neurotoxic.

**Fig 6 : Common Cobra**

## SNAKE VENOM APPARATUS

The typical snake venom delivery apparatus consists of bilateral venom glands situated below and behind the eyes and connected by ducts to hollow anterior maxillary fangs. In viperids (vipers and pit vipers), these fangs are long and highly mobile; they are retracted against the roof of the mouth when the snake is at rest and brought to an upright position for a strike. In elapids, the fangs are smaller and are relatively fixed in an erect position. Approximately 20% of pit viper bites and higher percentages of other snakebites (up to 75%

for sea snakes) are “dry” bites, meaning no venom is released. Significant envenomation probably occurs in ~50% of all venomous snakebites. Elapidae and Viperidae venom glands are located behind the eye which are surrounded by compressor muscles. At the base of fangs, venom duct opens where the venom are transported to its tip within a canal like a hypodermic needle. The snake can introduce the venom deep into the tissues of its prey with the help of its fang. In case of human bite, venom is usually injected subcutaneously or intramuscularly .Spitting cobras can squeeze its venom from their fangs like a fine spray directed towards the victim’s eye.

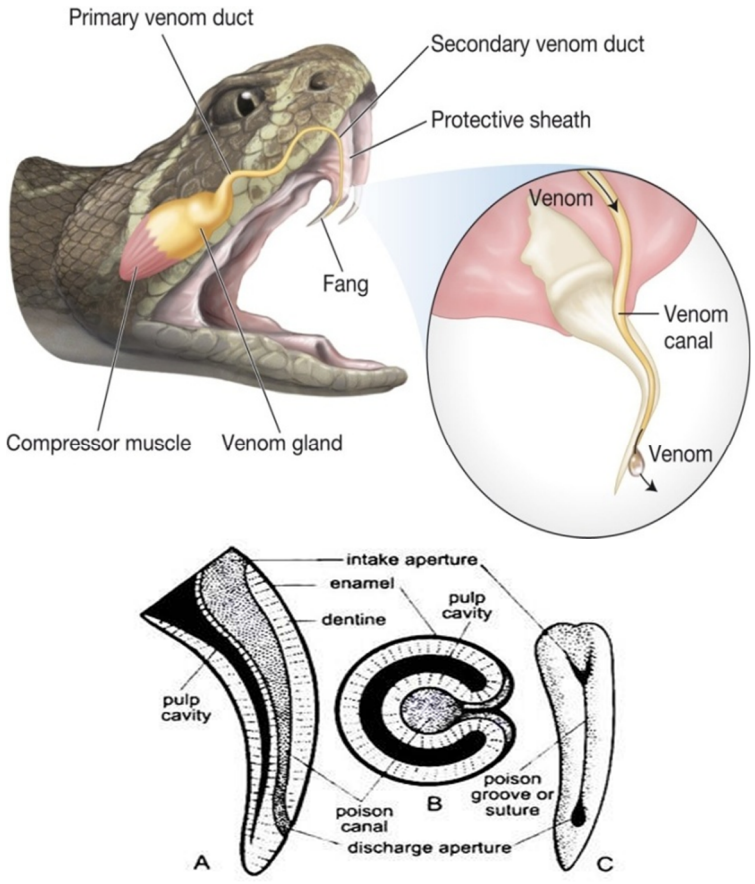



**Fig 7 : Snake Venom Apparatus**

**VENOMS**

Snake Venom is a complex fluid with powerful ingredients and is secreted by the parotid glands, mainly for immobilizing, killing & digesting small animals like rats. Snake venoms are highly variable and complex mixtures of enzymes, low-molecular-weight polypeptides, glycoproteins, and other constituents. Among the deleterious components are hemorrhagins that promote vascular leakage and cause both local and systemic bleeding Proteolytic enzymes cause local tissue necrosis, affect the coagulation pathway at various steps, and impair organ function. Hyaluronidases promote the spread of venom through connective tissue. Myocardial depressant factors reduce cardiac output, and bradykinins cause vasodilation and hypotension. Neurotoxins act either pre- or postsynaptically to block transmission at the neuromuscular junction, causing muscle paralysis. Most snake venoms have multisystem effects on their victims. Snake can bite once and continuously secrete the venom a number of times in succession. The lethal dose of the venoms for a man (Deoras 1965).

Cobra - 0.12 g

Krait–0.06g

Russell'sViper - 0.15 g

EchisCarinatus- 0.08 g

The concentration of venom shows diurnal and seasonal variation. Bites inflicted at night and immediately after hibernation are the most severe. In summer months the output of venom is more than in the winter, when the venom is viscous and comes out in small quantities. This may explain the high-

er mortality rate by Snake bites in the summer months including the monsoon. Most snakes inject about 10% of the available venom in single strike. It has the most complex of all venoms. More than 90% dry weight is protein comprising a rich variety of enzymes, non-enzymatic polypeptide toxins, and non-toxic proteins. Non-protein ingredients of venom include carbohydrates and metals (often in the form of glycoprotein metalloprotein enzymes), lipids, free amino acids, nucleotides, and biogenic amines. The lethal and more deleterious fractions of snake venoms are certain peptides and proteins of relatively low molecular weight (6,000 to 30,000). The peptides appear to have very specific receptor sites, both chemically and physiologically.

The polypeptide toxins (often called neurotoxins) are found most abundantly in elapid and hydrophid venoms. Postsynaptic alpha neurotoxins such as alpha bungarotoxin and cobrotoxin contain about 60 to 70 amino acid residues, and bind to acetylcholine receptors on the motor end-plate. Presynaptic beta neurotoxins such as beta-bungarotoxin, cobrotoxin, and taipoxin contain about 120–140 amino acid residues, and a phospholipase A subunit, and prevent release of acetylcholine at the neuromuscular junction. Cobra's alpha bungarotoxin, binds to the acetylcholine receptors and inhibits neural transmission at the neuromuscular junction. Krait's beta bungarotoxin causes an initial release of acetylcholine, but then damages the nerve terminal and prevents any further release. It is for this reason that krait victims often take longer to recover than cobra victims. The acetylcholinesterase found in most elapid venoms is no longer thought to contribute to their neurotoxicity.

Enzyme function and path physiological disturbances are most clearly related in the case of viper venom pro-coagulants. For instance, Russell's viper venom (RVV) contains at least two proteases, which activate the blood-clotting cascade. RVV-X, a glycoprotein, activates factor X by a calcium-dependant reaction, and also acts on factor IX and protein C. RVV-V, an arginine ester hydrolase, activates factor V. Echis venom contains a zinc metalloprotein "ecarin" which activates prothrombin. Russell's viper can induce neurotoxic symptoms in addition to haematological abnormalities. Many species of Russell's viper have this ability, and it is particularly evident in Southern India and Sri Lanka.

Hyaluronidase may serve to promote the spread of venom through tissues. Proteolytic enzymes (hydrolases) may be responsible for local changes in vascular permeability leading to oedema, blistering, and bruising, and to necrosis. Biological amines such as histamine and 5-hydroxytryptamine may contribute to local pain and permeability changes at the site of a snakebite.

Non protein ingredients of venom include carbohydrate and metals (often part of glycoproteins & metalloprotein enzymes) lipids, free amino acids, nucleosides and biogenic amines such as serotonin and Acetylcholine. About 80–90% of Viperidae & 25%to70% of Elapidae Venom consists of enzymes. The role of enzymes in envenoming is most clearly seen in the case of Venom procoagulants. For example, Vipera Russelli Venom contains.

| Enzymatic components in Snake Venom | |
|---|---|
| **ENZYME** | **EFFECTS** |
| Arginin hydrolase | Bradykinin release, interference with clotting |
| Collagenase | Digestion of Collagen |
| Hyaluronidase A | Reduction of Collagen Viscosity. Promotes the spread of venon through tissues |
| Phospholipase A | Uncoupling of oxidative phosphorilation |
| Phospholipase B | Hydrolysis of lysophosphatids |
| Phosphodiesterase | Inhibition of DNA, RNA, arabinose derivatives |
| Acetylcholinesterases | Catalysis hydrolysis of Ach. But this is no longer thought to contribute to their neurotoxicity |
| 5' nucleotidiase | Specific hydrolysis of Phosphate mono-esterases which links with 5 position of DNA, RNA |
| L-aminoacid oxidase | Catalysis of aminoacid oxidation gives colour of venom. |
| Thrombin, like enzyme | Depression of fibrinogen levels. |

| Non-Enzymatic components in Snake Venom | |
|---|---|
| **COMPONENT** | **EFFECTS** |
| Neurotoxins (elapidae) | Post synaptic non depolarizing neuromuscular. |
| Cobrotoxin | blockade of long duration, acting only on nicotinic acetyl choline receptors to some extend cardiotoxic. |
| Erabutoxin | Acetyl choline receptors to some extend cardiotoxic |
| Alpha Bungarotoxin | Haemotoxic and anticoaguland-blinds to receptors. |
| Cerelotoxin | Similar post synaptic block but without binding to receptors |
| BetaBungarotoxin<br>Crotoxin<br>Taipoxin | Pre-synaptic motor nerve end blockade |
| Haemorrhagins | Direct disruption of vessel endothelium |
| (HR-1,HR-2)<br>Viperidae, Crotalidae | Procoagulant effects – Factor IX activation by cleavage of peptide bond IX by Russell's, Factor X activation by Calcium binding to gammaglutamic residues in F.X with rapid change Xa, direct prothrombin activation by cleavage of peptide bonds by venom, producing an intermediate which quickly converts to thrombin. |

| Feature | Cobras | Kraits | Russell's Viper | Saw Scaled Viper | Hump Nosed Viper |
|---|---|---|---|---|---|
| Local Pain/ Tissue Damage | YES | NO | YES | YES | YES |
| Ptosis/ Neurological Signs | YES | YES | YES! | NO | NO |
| Haemostatic abnormalities | NO | NO! | YES | YES | YES |
| Renal Complications | NO | NO | YES | NO | YES |
| Response to Neostigmine | YES | NO? | NO? | NO | NO |
| Response to ASV | YES | YES | YES | YES | NO |

**Fig 8 : features of different snake bite**

## ALTERATION IN COAGULATION FOLLOWING SNAKE BITE:

Snake venom is complex toxin or poison. But it's mixture of various components such as proteins, enzymes, non-toxic proteins, nucleotides, carbohydrates, lipids, biogenic amines and nucleotides.

Russell's viper and Echis carinatus bites can result in defects in coagulation and bleeding. Viper venom contains many active substances, which can induce bleeding and induce clotting. Snake venom containing Hemorrhagin can damages the blood vessels directly, by loosening the gaps between the endothelial cells and thereby leading to the injury of the capillary basement membrane. Which in turn results in spontaneous bleeding .

In-vivo, large amount of venom leads to massive intravascular clotting, which can stop circulation and results in rapid death. But in case of snake bite the venom is less in quantity and it leads to continuous activation of fibrinogen which in turn produces fibrin which is fragile and more susceptible to lysis than the ordinary fibrin. As the venom destroys fibrinogen at a faster pace then liver produces, the blood tends to clot poorly or it fails entirely. The balance between this anticoagulants, procoagulants, fibrinogenolytic and fibrinolytic components of the injected venom determines the final state of coagulation disturbance.

Russell's viper venom selectively activates Factor X. Echis carinatus venom accelerate the conversion of prothrombin into abnormal thrombin and also activates Factor X. Thus the abnormal thrombin prevents the stabilization of fibrin and also promotes coagulation which is achieved by stimulation of plasminogen system and by inhibition of factor XIII activity. The result is similar to that of DIC, fibrinolysis and increased Factor V consumption. Viper poisoning usually shock and hemorrhage resolves within a week, but coagulation changes tend to persist for 2 weeks or longer in case the specific anti snake venom is not given on time. In more than 50 % of patients, Intravascular hemolysis was present amongst patient who presented with ARF- Acute renal failure, jaundice, anemia, reticulocytosis and hemoglobinuria and raised plasma free hemoglobin.

Platelet dysfunction and thrombocytopenia are commonly seen because of the various proteins present in this venom which can directly destroy the platelets and also can cause a functional impairment of the platelets.

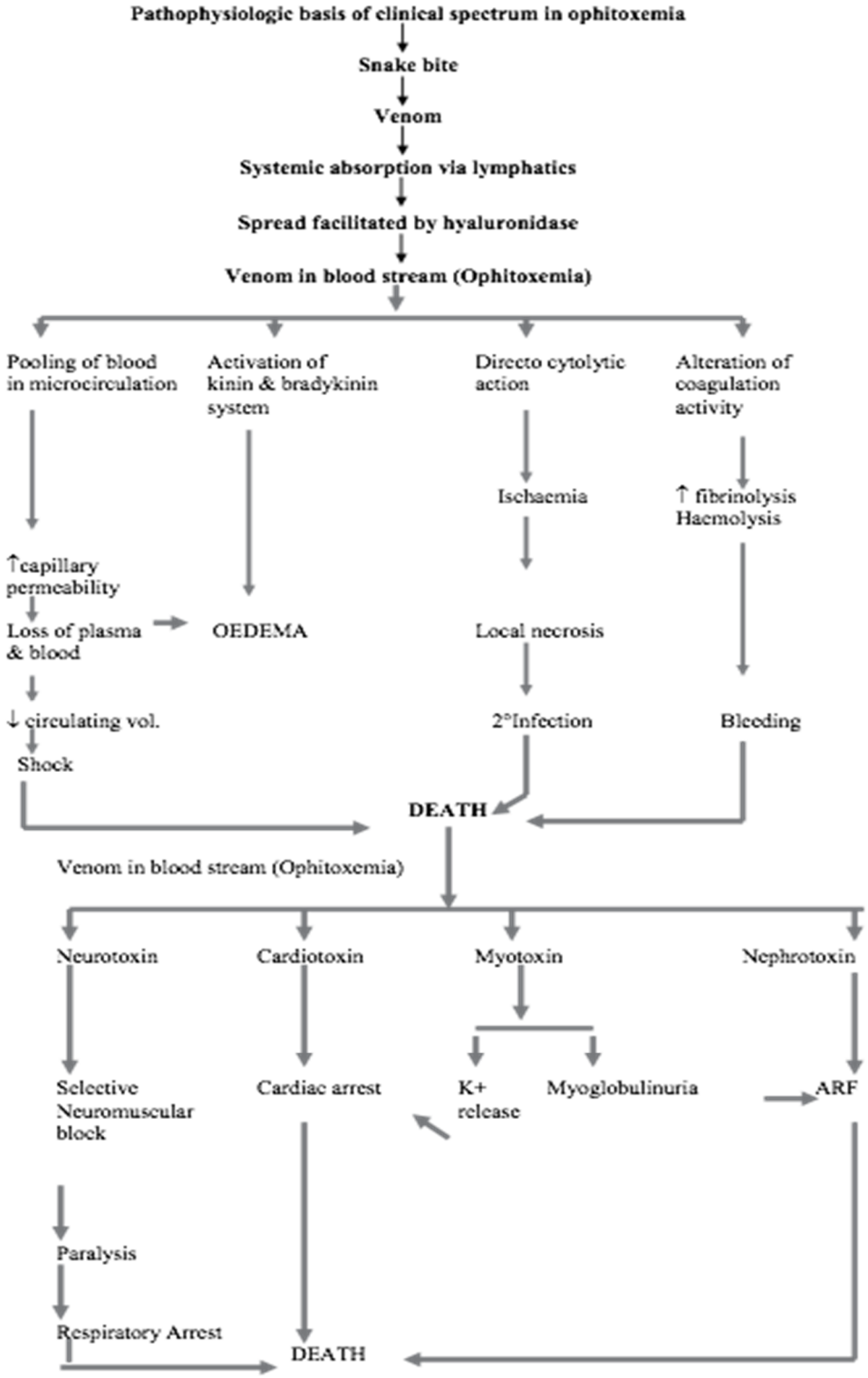
**Haemorrhagins (HR –1 & HR – 2)**

Haemorrhagins, two immunologically distinct non enzymatic haemorrhagic principles (HR – 1 & HR – 2) are typical components of Crotalid(Pit viper) and Viperid (true Viper) venoms. They cause acute, rapid haemorrhage. In many cases of serve envenomation, haemorrhagins play a lethal role by causing haemorrhage in the kidneys, heart, Brain, Lungs, and gastrointestinal tract. Pharmacologically, the haemorrhagins have been demonstrated to be separate entities from proteolytic enzymes in the venom.

The haemorrhagins act by directly disrupting the endothelial lining and by inhibiting platelet aggregation. Pharmacological studies have further shown that the haemorrhagic principles induce the release of certain autopharmacological mediators such as histamine and 5-HT from various tissues which open up endothelial cell junction and disrupt the isolated basement membrane, presumably in an enzymatic mode of action thus causing vascular damage and haemorrhage. Similarily vasculotoxic changes have also been observed in the renal and cerebral vessels with crotalid venom. The observed vasculotoxic changes resulting in severe cutaneous and systemic haemorrhage particularly in kidneys, lungs and brain bear a close resemblance to that of experimental schwartzman phenomenon with bacterial toxins

## PATHOGENESIS OF SNAKE BITE:

### Clinical Features



## NON-VENOMOUS SNAKEBITE

A significant proportion of snakebites is said to be due to non-venomous snakes. Since the question of envenomation does not arise in such cases, systemic manifestations are nonexistent, except those due to psychological shock. As a result of the fear and apprehension associated with snakes, every bite (venomous or otherwise) is attended by some degree of shock characterised by giddiness, syncope, sweating, palpitation, tachycardia, and hypotension. These emotional manifestations develop almost instantaneously and may produce psychological shock and even death. Fear of snake bite may cause also transient pallor, sweating and vomiting. Consequent upon reassurance especially by a doctor, about the non-venomous nature of the bite, these symptoms usually resolve rapidly.

## VENOMOUS SNAKEBITE

Based on the predominant constituents of venom, snakes were loosely classified as neurotoxic (notably cobras and kraits), vasculotoxic (vipers) and myotoxic (sea snakes). However it is now well recognized that such a strict categorization is not valid as each species can result in any kind of manifestations.

***Without Envenomation:***

a. 20 to 50% of venomous bites does not have serious toxicity.

b. The reasons for lack of envenomation in bites of venomous snakes are as follows:

- *Dry bite:* venoms are not always injected in every bite.
- *Protective gear:* bites inflicted on shod feet and heavily clothed parts, Envenomation may not occur .
- *Leakage of venom:* all or some of the venom escape outside the bite site when snake sidewipes.
- *Superficial bite:*. The snake often does not bite deeply deliberately, but instead only strikes superficially because humans are not normal prey for most of the snakes, thereby conserving precious venom for its genuine prey and they bite only to defend itself.

***With Envenomation:***

a. **Elapid Bite**

- Local Effects: Pain and swelling, serosanguinous oozing from the bite site with mild tenderness, and blistering. Cobras can sometimes cause significant local swelling, pain, blistering, and regional lymphadenopathy.
- Systemic Effects: The dominant clinical feature of elapid bites is Neurotoxicity. It can occur within 15 minutes to ½ hour in cobra bite, while krait bite it is often delayed up to several hours.

Pre-paralytic Stage

- Vomiting
- Ptosis
- Blurred vision

- Headache, myalgia
- Vertigo
- Paraesthesiae around the mouth
- Hypersalivation.

Paralytic Stage

- progressively flaccidly paralysed of facial muscles, vocal cords, neck muscles, palate, jaws, tongue, and muscles of deglutition.
- Respiratory arrest can occur due to paralysed tongue or inhaled vomitus, or paralysis of intercostals muscles and diaphragm.

Bedside tests to identify impending respiratory failure .

1. SINGLE BREATH COUNT : in one exhalation the number of digits counted - should be > 30 .
2. BREATH HOLDING TIME : Breath held in inspiration - normal count is > 45 second.
3. Ability to complete one sentence in one breath .

- Convulsions and loss of consciousness as result of chronic hypoxaemia.
- Roughly 50% of patients bitten by monocellate cobra(*Naja kaouthia* ) do not sustain envenomation.
- Rarely elapid bites cause renal failure.
- Rarely Disseminated intravascular coagulation may occur after Elapid bite.

b. **Viperid Bite**

- Local Effects:

local manifestations usually occurs within half an hour of bite, but may be delayed for several hours as well.

First Swelling will appears around the snake bite site, and then spreads to the adjacent area and quickly to involve the entire limb and adjacent trunk, associated with pain, tenderness, and regional lymphadenopathy.

In about 12 hours Blisters begin to appears around the bite site which subsequently progress to involve the entire limb. About 10 to 15% of the cases extensive necrosis of skin, subcutaneous tissues, and muscles can develope.

Raised intracompartmental pressure , causing compartment syndrome.

- Systemic Effects:

Haemostatic abnormalities are very characteristic. Evidence is first seen as persistent bleeding from the bite site. Within a few hours of the bite hematuria develops then gingival bleeding, then followed by epistaxis. Hours later bleeding into the floor of the mouth, haemoptysis, haematemesis, ecchymoses, intracranial and sub-conjuctival haemorrhages, and tympanic membrane, gastrointestinal tract, and genito-urinary tract bleed can occur. Few cases of Anterior pituitary bleeding has been reported. Hemiplegia, loss of consciousness, and convulsions can occur as a result of Subarachnoid and intracerebral haemorrhage may. Cases of Retroperitoneal and intraperitoneal haemorrhages have been reported.

Intravascular haemolysis producing haemoglobinuria and renal failure is a frequent occurrence, especially in Russell's viper bite .

Hypotension accompanied by tachycardia, unless the snake venom has affected the heart directly or reflexly.

Like Cardiotoxicity seen in elapid , it can also produces a wide variety of ECG.

Neurological symptoms may occur in the case of Russell's viper bite like ptosis, respiratory failure and paralysis.

**LIFE THREATENING COMPLICATIONS :**

- **ACUTE KIDNEY INJURY**

Acute kidney injury (AKI) is an important complication of snake bite and a major cause of mortality. AKI is common after bites from myotoxic or hemotoxic snakes. These snakes are Russell's viper, saw-scaled viper, hump-nosed pit viper, green pit viper, and sea-snake. Renal pathologic changes include tubular necrosis, cortical necrosis, interstitial nephritis, glomerulonephritis, and vasculitis. Hemodynamic alterations caused by vasoactive mediators and cytokines and direct nephrotoxicity account significantly for the development of nephropathy. Hemorrhage, hypotension, disseminated intravascular coagulation (DIC), intravascular hemolysis, and rhabdomyolysis enhance renal ischemia leading to AKI[23]. The incidence of AKI caused by these snakes varies from 5% to 29% depending on the species of snake and the severity of envenomation[24-26]. The onset of AKI is from a few hours to as late as

96 h after the bite. The duration of AKI after snake bite generally ranges from 2 to 3 wk. Tubular necrosis is an important pathological correlate of AKI. Prolonged AKI with oligoanuria after snake bite is indicative of cortical necrosis or acute tubular necrosis associated with interstitial nephritis or extracapillary glomerulonephritis[23].

**LONG TERM COMPLICATIONS OF SNAKEBITE**

1. Chronic ulceration, osteomyelitis, arthritis.
2. Malignant transformation (Marjolin's ulcer) .
3. Chronic kidney disease.
4. Hypopituitarism or Diabetes Insipidus may occur after Russell's viper bite.
5. Chronic neurological deficits in patients who survive intracranial haemorrhages and thrombosis.
6. Psychological disturbances such as depression, anxiety, post traumatic stress disorder.
7. Chronic musculoskeletal disabilities such as muscle wasting, stiff joints, impaired balance, fixed deformities may occur.

**OCCULT SNAKE BITE** :

Identification of Krait bite marks is difficult as Krait has fine slender teeth and a nocturnal habitat. Sometimes in the early morning patient may come with complains of paralysis with no other symptoms in Krait bite cases. They will have typical history of going to bed at night and getting up in the morning with severe epigastric pain and vomiting following which the patient developed neuroparalytic symptoms with no history of snake bite. Krait bite produces descending neuroparalysis whereas GBS produces ascending paralysis.

**FIRST AID MEASURES** :

- History of snake bite should be checked and evidence of snake bite like fang marks , bleeding , swelling of bitten part should be check .

**HISTORY :**

a) history about the events occurred during bite and the progression of local and systemic symptoms and signs.

b) Many of the non venomous species leave just two fang-like marks on biting, so Bite marks are of little importance.

c) To Determine the exact time of snake bite. As in case of early presentation of snake bite, the patient may have only few symptoms and signs even with large amount of venom has been injected.

d) Patient should be asked about the quantity of urine he passed. Patients with neurotoxic envenomation may complains of drooping of eyelids, blurring of vision, double vision or sleepiness.

e) As far as possible the snake responsible must be identified.

f) History of any traditional medicine was used for snake bites before reaching hospital as it can cause problems and produce symptoms that confuse the diagnosis.

- Reassured to patients that 70% of all snakebites are non-venomous snakes.
- Limb rest and immobilization using bandage or cloth to hold the splint without blocking the blood supply.
- Discard Traditional first aid measures as it will do more harm to patients.
- Loosening and removing all Tight objects like clothing, shoes, watches, rings since it can increase the swelling.
- Anti Snake Venom should not be injected locally.
- Tourniquet must be avoided as it may cause gangrene.

The mnemonic recommended for snake bite, first aid " Do it R.I.G.H.T " which is

R = Reassure the patient as 70% snake bites are non venomous and only 50% of bites by venomous species envenomate the patient.

I = Immobilize the limb in the same way for fractured limb.

GH = Get to Hospital immediately. Traditional remedies should be avoided.

T = Tell the doctor about any systemic symptoms such as ptosis that manifest on the way to hospital.

**ASSESSMENT**:

Time since the snake bite should be determined.

Any Medical history like presence of systemic diseases, allergy, use of medication.

**PHYSICAL EXAMINATION:**

Patient should be monitored closely, the following parameters:

- Pulse rate
- Respiratory rate
- Blood pressure
- Oxygen saturation
- 20 minutes Whole Blood Clotting Time, every hour for first 3 hours and every 4 hours for next 24 hours .

- Examination of distal pulses and capillary filling time in the presence of gross swelling. Pain on passive movement, pallor , pulse less limb, hypoesthesia one should suspect the diagnosis of compartment syndrome . Compartment pressure is measured by inserting a 16 G IV cannula and connecting it to manometer if it reads above 40 cm water then the diagnosis of compartment syndrome should be made.

**EARLY SIGNS OF SEVERE ENVENOMING:**

- Rapid extension of local swelling.
- Early tender enlarged lymph nodes, indicates the spread of venom to lymphatic.
- Neurological signs like ptosis, neck muscle weakness and respiratory distress .
- Bleeding manifestations like bleeding from bite site, gums, ecchymoses, haematuria, hemoptysis and epistaxis.
- Dark brown urine.

**LAB TEST**S:

20 MINUTE WHOLE BLOOD CLOTTING TIME (20 WBCT):

Prothrombin time

**OTHER TESTS:**

a. Complete Blood Count

b. Prothombin time

c. Liver function test

d. Renal Function test

e. Blood sugar

f. ECG

g. Abdominal ultrasound

**Anti Snake Venom(ASV)**:

1. ASV is the only specific antidote for snake bite.
2. No absolute contraindication to ASV.
3. ASV may reverse systemic envenomation.
4. Polyvalent ASV is available in India which is effective against all four common species (Russell's Viper, Common Cobra , saw -scaled viper and common Krait).
5. ASV are produced in two forms liquid and lyophilized forms. Liquid ASV should be stored in cold chain and has shelf life of 2 years. Lyophilised ASV, in powder form, has shelf life of 5 years and can be stored in cool place.
6. Anti Snake Venom contains equine immunoglobulin fragments F(ab')2 prepared from plasma of horses immunised with venom of one or more snake species.

7. Anti Snake Venom can be either Monovalent or Polyvalent. Monovalent ASV neutralizes, venom of only one snake species whereas Polyvalent ASV neutralizes the venom of several different snake species.
8. One ml of polyvalent ASV has the capacity of neutralizing the venomof the following:
    a. 0.60mg of dried Indian Cobra (Naja naja) venom.
    b. 0.45mg of dried Common Krait (Bungarus Caeruleus ) venom .
    c. 0.60mg of dried Russell's Viper (Daboia russelii ) venom.
    d. 0.45mg of dried Saw-scaled viper (Echis carinatus) venom .
9. The antitoxic equine Immunoglobulin are obtained from the serum of healthy equines which are immunized against venoms of various snake species.
10. ASV must be given only by Intravenous route, and should be given slowly.
11. Adrenaline should always be kept ready before ASV is administered.
12. ASV should not be given by Intramuscular route due to poor bioavailability.

**DOSE OF ASV FOR NEUROPARALYSIS:**

For Neuroparalysis 10 vials of Anti Snake Venom is given as IV infusion over 30 minutes. Second dose of 10 vials can be given if there is no improvement within 1 hour. Maximum dose of 20 vials can be given.

**DOSE OF ASV FOR VASCULOTOXIC SNAKE BITE.**

Two regimens are followed for vasculotoxic snake bite.

- Low Dose infusion therapy:

10 vials of ASV for Russel's Viper ; 6 vials of ASV for saw scaled viper as a stat infusion over 30 minutes followed by 2 vials of ASV for every 6 hours as an infusion in 100 ml of normal saline , till the clotting time normalizes or for 3 days whichever is earlier.

- High bolus therapy:

10 vials of ASV as a stat over 30 minutes as an infusion followed by 6 vials of ASV every 6 hourly as a bolus until clotting time normalizes .The amount of venom injected is about 5mg to 14.7mg. The maximum Anti Snake Venom dose is 30 vials since each vial neutralizes 6mg of Russell's viper venom .

**ASV REACTION :**

Anti Snake Venom test dose is not needed.

Some patients may develop anaphylaxis, characterized by hypotension, bronchospasm, and angioedema .

**EARLY ANAPHYLACTIC REACTION TO ASV**

Occurs within 10 to 180 min of starting ASV. They may present with itching, urticaria, dry cough, nausea, vomiting, abdominal colic and tachycardia.

**PYROGENIC REACTIONS**

Develops within 1 to 2 hours after treatment, patient may present with fever, chills and rigors and hypotension.

Any new onset of sign or symptom after starting the Anti Snake Venom should be considered as ASV reaction.

**LATE REACTIONS TO ASV**

It develops within 1 to 12 days of treatment initiation. They presents with fever, vomiting, diarrhea, urtricaria, arthralgia, myalgia, nephritis and encephalopathy rarely.

**TREATMENT OF EARLY ASV REACTION :**

1. Adrenaline must be given intramuscular, an initial dose of 0.5mg for adults. Adrenaline has been proven safe in pregnant women, but anaphylaxis can induce abortion. Since life threatening anaphylaxis evolve very rapidly, adrenaline must be given at the very first sign of ASV reaction. Dose must be repeated in every 5 to 10 minutes, if the reaction persists or worsen.
2. Antihistamine like Chlorpheniramine maleate should be given through intravenous route over few minutes.
3. Hydrocortisone can be given through intravenous route.

**UNRESPONSIVE TO INTRAMUSCULAR ADRENALINE IN ANAPHYLAXIS**

1. Some patients who don't respond to the repeated doses of adrenaline, and who remain shocked must be made to laid supine and, with their legs elevated above the ground, the patient also be given intravenous volume replacement with 0.9% saline , usually 1-2 liters rapidly .
2. Adrenaline should be given as IV infusion [adult dose 1 mg in 250ml of 5% dextrose / 0.9% saline in 4 ugm /ml concentration; infused at 1-4 ugm/minute at 15 to 60 drops/min). Infusion rate can be increased up to 10 ugm/min.
3. If the patient still remains in shock, a vasopressor agent like Dopamine should be administered at the rate of 2-5 ugm/kg/min.

**RECURRENT SYSTEMIC ENVENOMATION:**

In some cases systemic envenomation has been observed in 24 to 48 hours of initial recovery, probably due to continuous absorption of venom from the bitten site which occurs after improvement in blood supply, following correction of shock and hypovolemia, and also after the disappearance of Anti Snake Venom from the circulation. This kind of cases are rare in India due to the prolonged half-life of polyvalent Anti Snake Venom. Also due to redistribution of venom from tissue into vascular space as a result of ASV therapy. So ideally watch out for recurrent envenomationt by observe the patient for the next 48 hours after the recovery.

## ACUTE KIDNEY INJURY

## DETECTION OF ACUTE KIDNEY INJURY

- ✓ When Urine output is < 0.5ml/kg/hr for > 6 hours.
- ✓ When Increased in Creatinine concentration >0.3 mg/dl or increasing by 1.5 to 2 times from the baseline Creatinine value.
- ✓ Clinical "Uraemia syndrome" defined by nausea, vomiting, hiccups, drowsiness, acidotic breathing, flapping tremor, pericardial friction rub, muscle twitching and signs of hypervolumia.

## TREATMENT OF ACUTE KIDNEY INJURY

Conservative management will avoid the need of renal replacement therapy.

If the patient has postural hypotension suggestive of intravascular volume depletion, the following should be given:-

1. Intravenous access.
2. Cautious fluid in adult patient should be given. About 250-500 ml of isotonic saline challenge be given over 1 hour and the patient must be closely monitored for the development of pulmonary edema. Fluid must be stopped if there are signs of pulmonary edema.
3. If there is no improvement in urine output then Frusemide stress test must be performed. Once adequate fluid replacement is given to the patient, 1 to 1.5mg/kg of Frusemide should be given slowly through intravenous route

at the rate of 4-5mg/minute and urine output should be monitored for 2 hours. If the output is less than 200 ml in 1 hour, then it denotes the progression to acute renal injury. If there is no improvement in output of urine despite these challenge, diuretics should be stopped and fluid intake should be restricted and should be promptly referred to a renal unit .

4. Patients with Acute renal injury should be monitored daily for urine output, urea, creatinine, electrolytes, pH, bicarbonate, calcium and phosphate.

**INDICATION FOR DIALYSIS**

1. Clinical uraemia like encephalopathy, pericarditis, gastrointestinal bleed and pulmonary oedema.
2. Patients with hypervolumia and not responding to diuretics.
3. Severe Hyperkalemia; plasma potassium > 7mmol/l.
4. Sever Symptomatic Acidosis.
5. Serum Creatinine > 4mg/dl ; blood urea > 130 mg/dl

**OCCUPATIONAL RISK AND OTHER ECOLOGICAL FACTORS:**

The normal perception is that rural agricultural workers are most at risk and the bites occur first thing in the morning and last thing at night. However, this is of very little practical use to rural workers in preventing snake bite since it ignores the facts.

In rubber, coconut and arecanut plantations, clearing the base of the tree to place manur causes significant number of bites.

- Harvesting high growing crops like Millet which requires attention focused away from the ground.
- Rubber tapping in the early hours – 03-00 a.m. to 06-00 a.m.
- Vegetable harvesting and fruit picking
- Tea and coffee plantation workers are at risk of arboreal and terrestial vipers bite when picking or tending bushes
- Clearing weeds, exposes workers to the same danger as their grass cutting colleagues.
- Walking at night without a torch, barefooted accounts for a significant number of bites.
- And Bathing in ponds, streams and rivers, in the evening. Cobras and other venomous species are good swimmers and may enter the water to hunt so one should not be assumed that because the victim is bitten in water that the species is non poisonous.

Walking along the edge of water ways.

**PREVENTIVE MEASURES**:

- To wear Closed type footwear at night along with a flashlight which is switched on.
- Carrying a stick when grass cutting, clearing the tree base and fruit picking.

- While collecting wood, Paying close attention to the leaves and sticks on the ground.
- Avoid Keeping the rubbish and animal feeds near the house since they may attract rats which are the prey for the snakes.
- Avoiding a sleep on the ground.

**Extrinsic, Intrinsic and Common Coagulation pathway-**

A basic understanding of coagulation pathway is required to interpret prothrombin time result. The Prothrombin time is measure of the integrity of extrinsic and common pathways of coagulation cascade. This consists of tissue factor and factor V, II(Prothrombin), V, X and fibrinogen. The test is performed by adding calcium and thromboplastin, an activator of the extrinsic pathway to the blood sample then measuring the time (in seconds) required for blood clot formation.

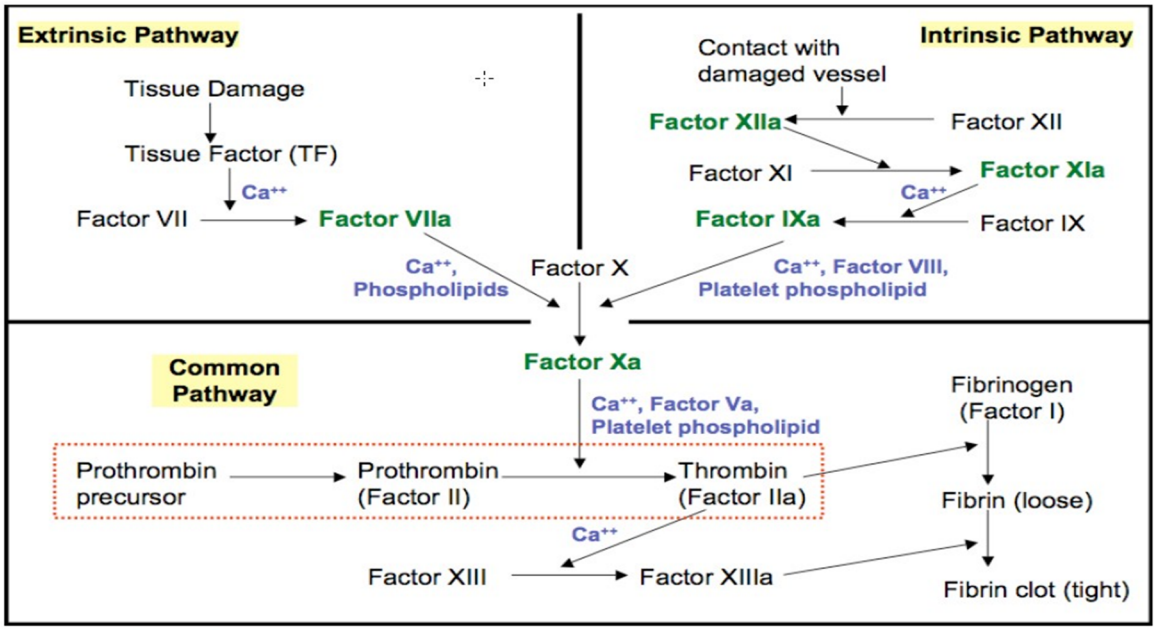
**Clotting time**

Clotting time is the time required for a sample of blood to coagulate in vitro under standard conditions.

There are various methods for determining the clotting time, the most common being the capillary tube method. Normal value of clotting time is 5 to 8 minutes. It is affected by calcium ion levels. Other methods for measuring clotting time are slide method.

Clotting is a natural defence mechanism to prevent blood loss from the body. A clot is usually formed within 5 minutes after injury. Whenever a blood

vessel is cut there is a rush of platelets causes a cut or injury to be filled and thus bleeding stops.




**Extrinsic, Intrinsic and Common Coagulation pathway**

**Clotting time test-**

In order for blood to clot, the enzyme thrombin must be generated from the plasma precursor prothrombin. Thrombin then converts soluble fibrinogen into insoluble fibrin. Generation of thrombin involves the sequential activation of a number of other plasma clotting factor, this process is also being assisted by $Ca^{++}$ and by factors released by platelets and damaged tissues . The time taken for blood to clot mainly reflects the time required for the generation of thrombin in this manner. If the plasma concentration of prothrombin or of some of the other factors is low (or if the factor is absent, or functionally inactive), clotting time will be prolonged.

## "WHOLE BLOOD COAGULATION (CLOTTING) TEST (LEE-WHITE)"

**Principle**: The whole blood clotting test is a rough measure of all intrinsic clotting factors in the absence of tissue factors. Variations are wide and the test sensitivity is limited. Whole blood, when removed from the vascular system and exposed to a foreign surface, will form a solid clot. Within limits, the time required for the formation of the solid clot is a measure of the coagulation system.

### 20 Minute Whole Blood Clotting Test

The 20 Minute Whole Blood Clotting Test provides a simple method of testing for coagulopathy in the envenomed patient, in circumstances where more sophisticated hematology is unavailable.

The equipment needed for the test consists of:

- Cotton wool or gauze pad
- Sterile syringe and needle
- Gloves
- Sharps disposal container
- Sterile (or clinically clean) 10ml test tube or which should be dry and should not be washed with soap.
- Clock or watch

**PROCEDURE**

Following normal venepuncture procedure, take 20ml of venous blood from the patient and place in the bottle.

Replace the lid of the bottle.

Place the bottle in a safe location, where it is not likely to get bumped or knocked over. The location of the bottle should be as close to room temperature as conditions allow.


Wait twenty minutes for the blood to clot. During this time do not shake the bottle or disturb the contents in any way.

After twenty minutes, gently invert the bottle, observing the contents. From this procedure it should be evident whether or not the blood has clotted.

Clotted blood is a negative result, indicating that there is no coagulopathy present. Blood which remains unclotted after 20 minutes shows the presence of coagulopathy. This does not, however, indicate whether the cause is a procoagulant or anticoagulant.

**Limitations-**

(a) The following variables tend to decrease the clotting time:

1) Rough handling of the blood specimen,

2) Presence of tissue fluids (traumatic venipuncture)

3) Frequent tilting of the tube, and unclean tubes.

(b) The following variables tend to increase the clotting time:

1) Extreme increases in temperature,

2) Variation in pH

3) Performance of the test at room temperature.

(c) This test is of value primarily as it was used to follow heparin therapy. Its use as a screening procedure is limited due to its poor sensitivity.

(d) The whole blood clotting time is affected mainly by defects in the intrinsic pathway factors and by defects in fibrin and fibrinogen. It is not sensitive to platelet abnormalities.

(e) A prolonged clotting time immediately indicates impaired coagulation, but a normal clotting time does not exclude many serious clotting defects.

(f) One disadvantage of the whole blood clotting time is its relative lack of reproducibility.

(g) This procedure has been replaced in most laboratories with the PT, which is more reproducible and easily controlled.

(h) The coagulation time is normal in thrombocytopenic purpura.

This is explained by the fact that only a small number of thrombocytes need be present for normal coagulation to take place.

**SUMMARY**

(1) A standardized test for determination of clotting time is described.

(2) It is easily performed by untrained workers with inexpensive material, and gives reproducible and accurate results.

(3) Since the possibility of subjective error is minimal, comparison of the results of different workers is possible

PROTHROMBIN TIME

The prothromb in time (PT) tests the adequacy of the extrinsic and common coagulation pathways. It represents the time needed for plasma to clot in the presence of an exogenously added source of tissue thromboplastin (e.g., brain extract) and $Ca^{2+}$ ions. A prolonged PT can result from a deficiency of factors V, VII, or X, prothrombin, or fibrinogen.

**Normal range**

The reference range for prothrombin time is 12-13 seconds. The normal values listed here-called a reference range-are just a guide. These ranges vary from lab to lab.

**METHODOLOGY**

A sample of the patient's blood is obtained by venepuncture. The prothrombin time is most commonly measured using blood plasma. Blood is drawn into a test tube containing liquid sodium citrate, which acts as an anticoagulant by binding the calcium in a sample. The blood is mixed and then centrifuged to separate blood cells from plasma. In newborns, a capillary whole blood specimen is used.

The plasma is analyzed by a biomedical scientist on an automated instrument at 37°C, which takes a sample of the plasma. An excess of calcium is added (there by reversing the effects of citrate), which enables the blood to clot again. For an accurate measurement the proportion of blood to citrate needs to be fixed; many laboratories will not perform the assay if the tube is under filled and contains a relatively high concentration of citrate. If the tube is under filled or overfilled with blood, the standardized dilution of 1 part anticoagulant to 9 parts whole blood is no longer valid. For the prothrombin time test the appropriate sample is sodium citrate tube, which is a liquid anticoagulant.

Tissue factor (also known as factor III) is added, and the time the sample takes to clot is measured optically. Some laboratories use a mechanical measurement, which eliminates interferences from lipemic and icteric samples. The patient's results are not regarded as abnormal unless the clotting time is more than two seconds longer than the control time. The prothrombin ratio is the prothrombin time for a patient, divided by the result for control plasma. The upper limit of normal is 1.2.

Prothrombin time (PT) is a blood test that measures how long it takes blood to clot. A prothrombin time test can be used to check for bleeding problems. PT is also used to check whether medicine to prevent blood clots is working.

In addition to sensitivity to prothrombin levels, the test detects deficiency of factors V, VII, X, fibrinogen and presence of some inhibitiors. When it is necessary to distinguish between factor deficiencies and the presence of inhibitors, the test is repeated on the patient's plasma after adding a small volume (20%) of normal plasma; the clotting time is almost completely corrected when the clotting abnormality is due to deficiency, but is poorly corrected when inhibitors are present[44].

The prothrombin time is prolonged due to-

- Low levels of blood clotting factors.
- A change in the activity of any of the clotting factors.
- The absence of any of the clotting factors.

**ACTIVATED PARTIAL THROMBPLASTIN TIME(aPTT):**

- This tests abnormalities of all coagulation factors except factors VII and XIII. This test is especially sensitive for early stage of intrinsic pathway. The test is performed with 0.1 ml of test plasma 0.1 ml of liquicelin reagent solution is mixed for 3 minutes at 37 c in water bath. 0.1ml of pre-warmed calcium chloride was added and stop watch started end point recorded. Abnormal values should exceed control values by 6 seconds. More than 10 seconds is definitely abnormal.

# MATERIALS AND METHODS

**SOURCE OF STUDY:**

Data consists of primary data collected by the principal investigator directly from the patients who are admitted in the Coimbatore Medical College and Hospital.

**DESIGN OF STUDY**: retrospective cohort Study.

**PERIOD OF STUDY**: One year, Feb 2017 - Feb 2018.

**SAMPLE SIZE**: 100

**INCLUSION CRETERIA:**

1. All snake bites with suspected envenomation.
2. Definitive fang mark present in cases with history of snake bite.
3. Adult between the age of 15-45 years of age.
4. Consented for participation.
5. Within 6 hours of snake bite.

**EXCLUSION CRITERIA:**

1) Sepsis and DIC

2) Acute and chronic liver diseases

3) Anti coagulation therapy: Warfarin, Heparin

4) Any case of coagulation disorder.

5) Pregnant women and mentally-ill.

6)Any patient with pre thrombotic disease

## METHODOLOGY

The study is will be undertaken on the patients admitted in the Coimbatore Medical College and Hospital with history of snake bite, during the study period (Feb 2017 to Feb 2018). A total of 100 patients with history of snake bite and definitive bite marks present , presenting within 6 hours of snake bite.

The study is proposed to be conducted after obtaining informed signed consent from the patients and after obtaining approval from ethical committee . The duration of the study is one year from Feb 2017 to Feb 2018. The principal investigator, after obtaining proper informed signed consent from the patients to participate in the study, collects their details, medical history details, physical examination details and blood samples .

Any snake bite case with a definitive bite mark present , blood sample for evaluation of whole blood clotting time, PT , aPTT and INR to be collected and to labeled the time at collection. The total number of ASV vials given was noted.

Complications were defined as:

1. 1.ACUTE KIDNEY INJURY : Serum creatinine > 1.5 mg/dl or oliguria < 400ml/day .
2. Disseminated intravascular coagulation.
3. Compartmental syndrome , gangrene, cellulitis that required debridement.

4. Shock, sepsis .
5. Neurological paralysis requiring ventilatory support.

**INVESTIGATIONS:**

1. PT .
2. aPTT .
3. INR
4. whole blood clotting time.
5. Liver Function Test
6. ECG
7. Complete blood count

## STATISTICAL ANALYSIS

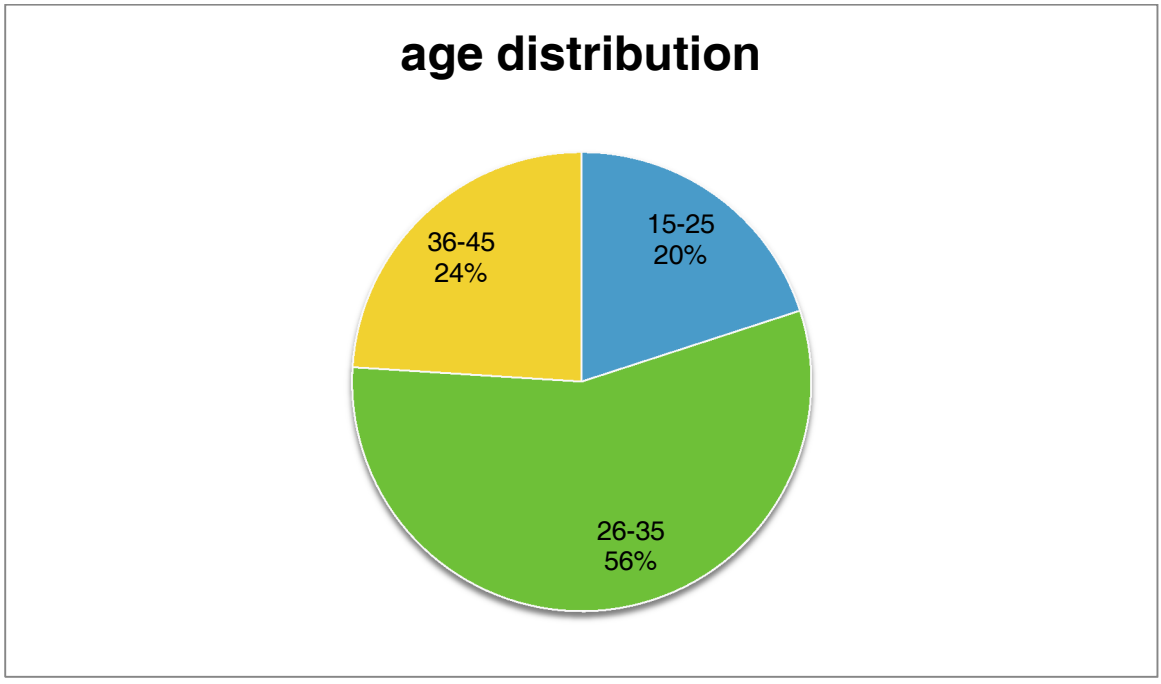
Using EXCEL 2007 Software all data collected were entered and analysed. Nominal data's were converted into numerical values and the analysed. Numerical values were reported using mean and standard deviation or median. A Confidence interval of 95 % was taken. Probability value (p) value less than 0.05 was considered a statistically significant.

# RESULTS

**Table : 2.1 AGE DISTRIBUTION**

| AGE (IN YEARS) | NO OF PA-TIENTS | PERCENTAGE |
|---|---|---|
| 15-25 | 20 | 20% |
| 26-35 | 56 | 56% |
| 36-45 | 24 | 24% |

**Chart : 2.1 AGE DISTRIBUTION**

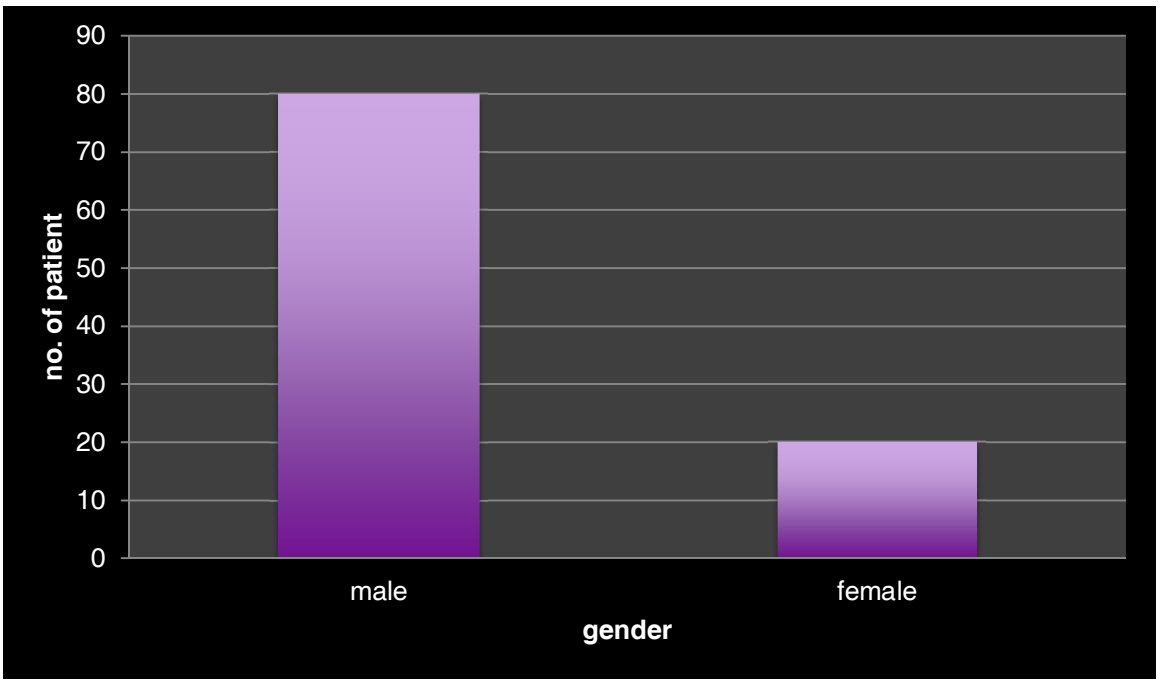



Majority of the cases were of the age group of 26-35 years of age, which constituted 56%.

**Table : 2.2 SEX DISTRIBUTION:**

| SEX | NO OF PATIENTS | PERCENTAGE |
|---|---|---|
| MALE | 80 | 80% |
| FEMALE | 20 | 20% |

**Chart : 2.2 SEX DISTRIBUTION:**

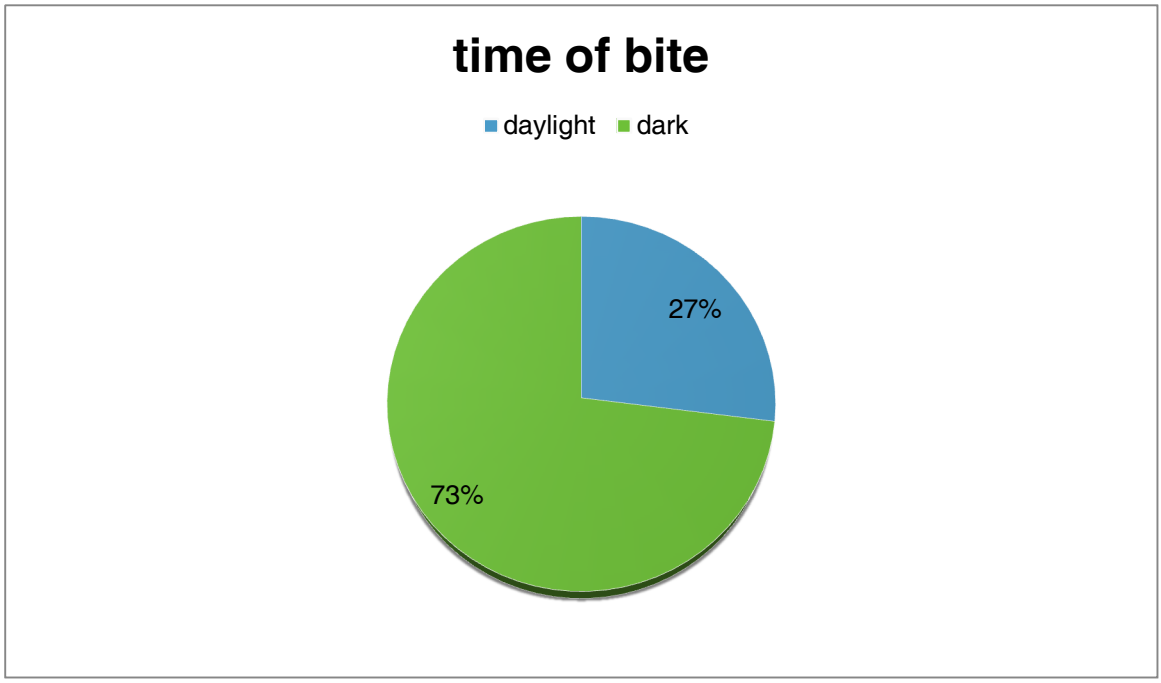



Majority of the cases, that is 80% of the study group were male.

**Table : 2.3 TIME OF BITE :**

| Time of bite | No. of persons |
|---|---|
| daylight | 27 |
| dark | 73 |

**Chart : 2.3 TIME OF BITE :**

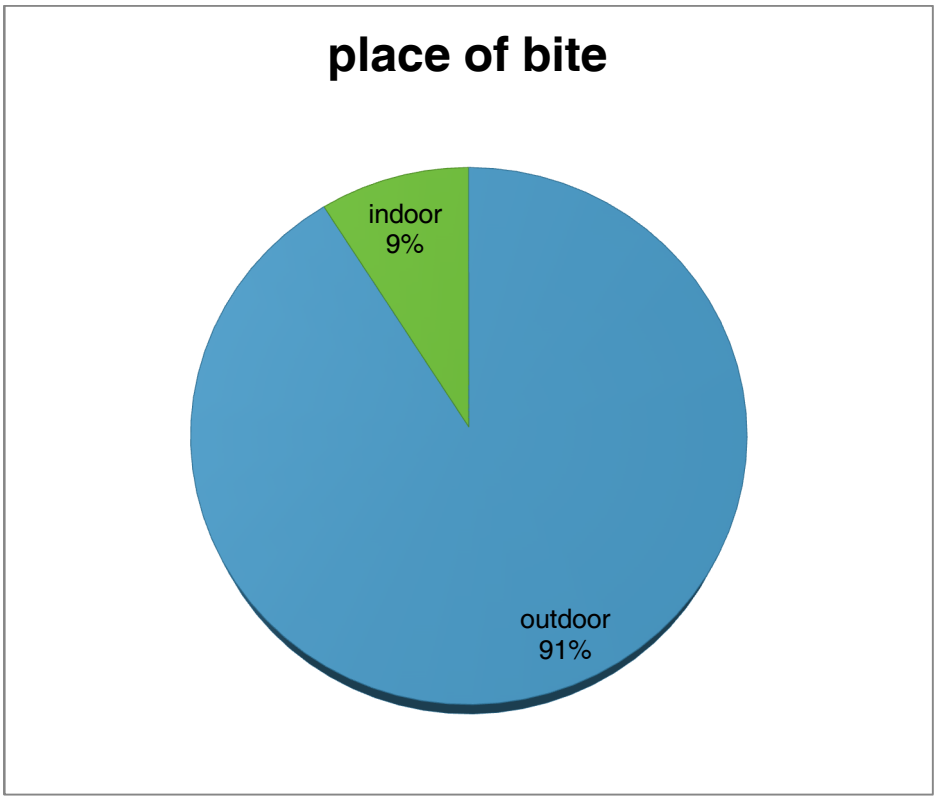



73 % of the cases were bitten in the dark.

**Table : 2.4 PLACE OF BITE:**

| Place of bite | NO OF PATIENTS |
|---|---|
| Outdoor | 91 |
| Indoor | 9 |

**Chart : 2.4 PLACE OF BITE**

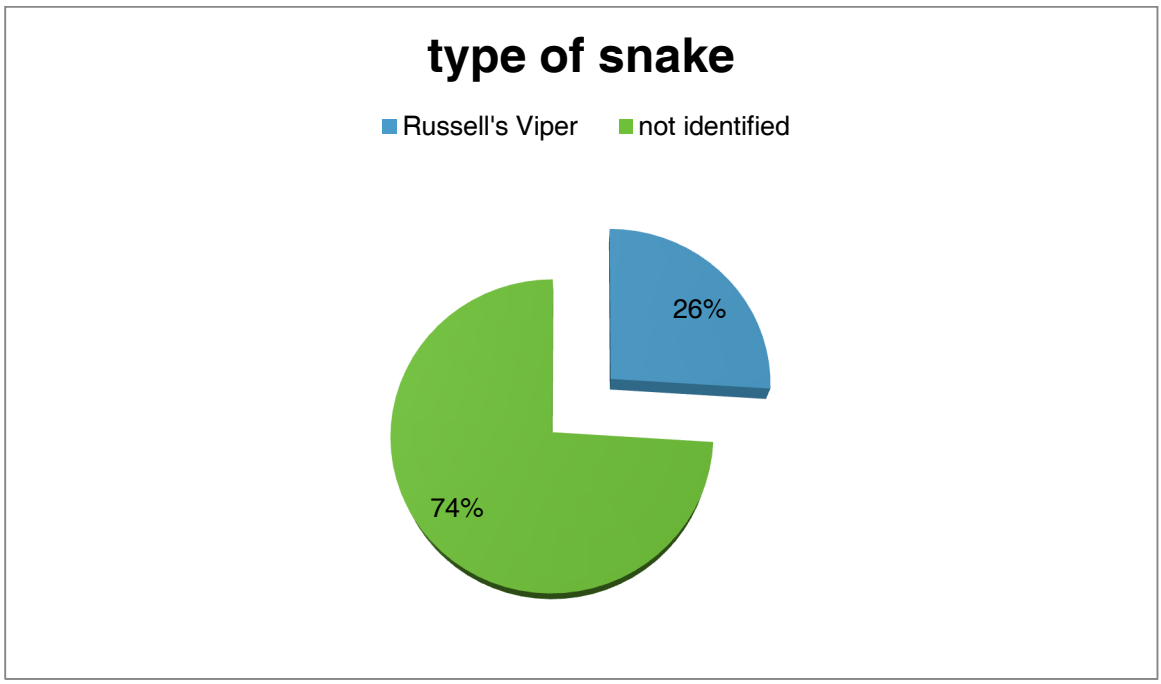



Maximum cases occurred out doors.

**Table : 2.5 TYPE OF SNAKE:**

| Type of snake | No. of people |
|---|---|
| Russell's Viper | 26 |
| Not identified | 74 |

**Chart: 2.5 TYPE OF SNAKE:**

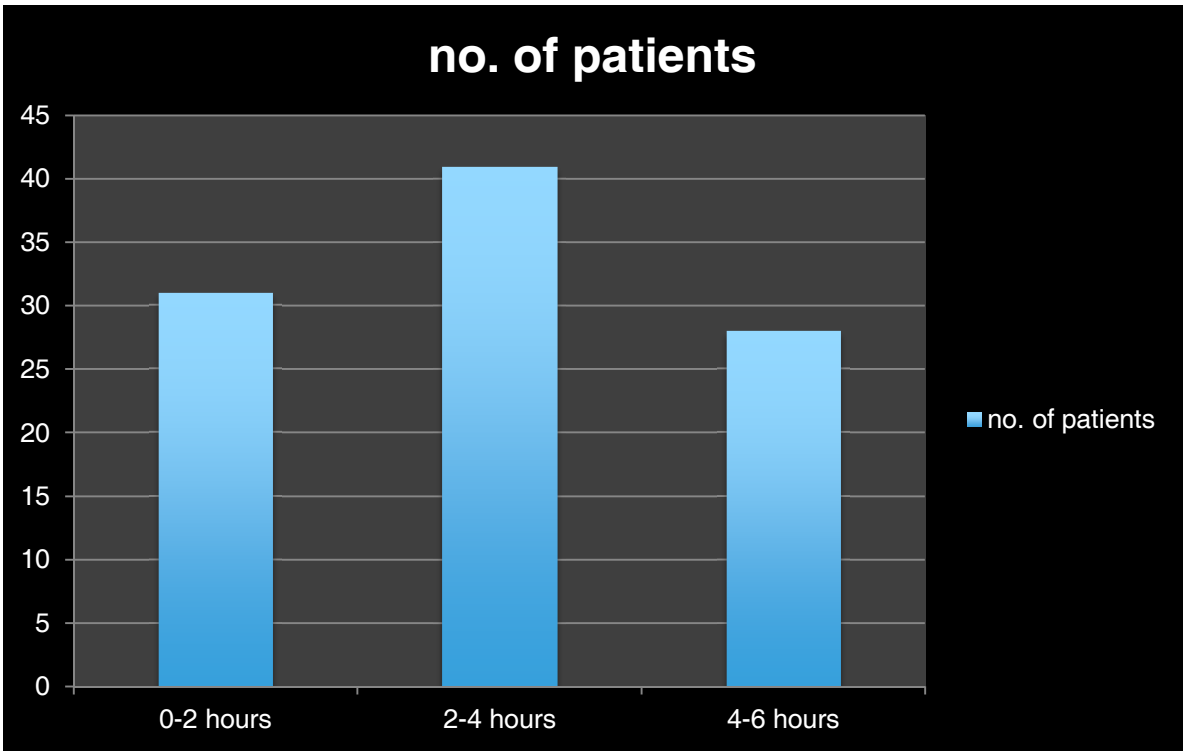



In Most of the cases, snake could not be identified ie. 74% and 26 % was identify as Russell's Viper.

**Table : 2.6 BITE TIME TO PRESENTATION**

| BITE TO TIME of PRESENTATION | NO. OF PATIENTS |
|---|---|
| 0-2 HOURS | 31 |
| 2-4 HOURS | 41 |
| 4-6 HOURS | 28 |

**Chart : 2.6 BITE TIME TO PRESENTATION**

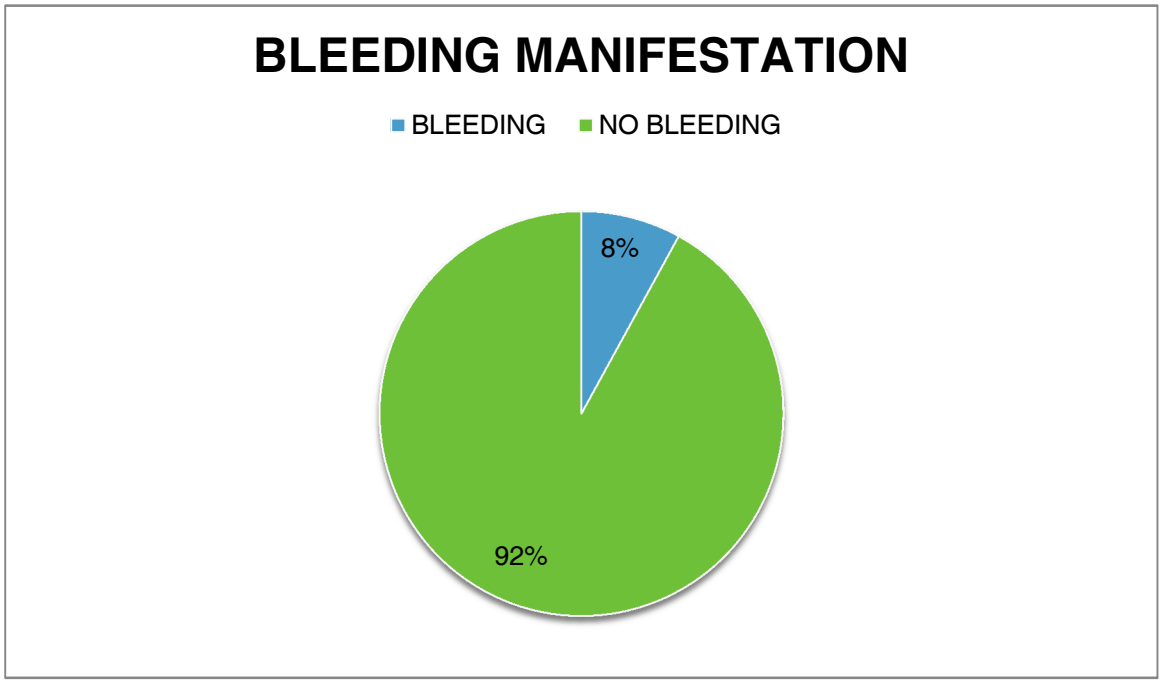



Majority of the cases reported within 2-4 hours of snake bite.

**Table : 2.7 BLEEDING MANIFESTATION AT PRESENTATION**

| BLEEDING MANIFESTATION | NO. OF PATIENTS |
|---|---|
| BLEEDING | 8 |
| NO BLEEDING | 92 |

**Chart : 2.7 BLEEDING MANIFESTATION AT PRESENTATION**

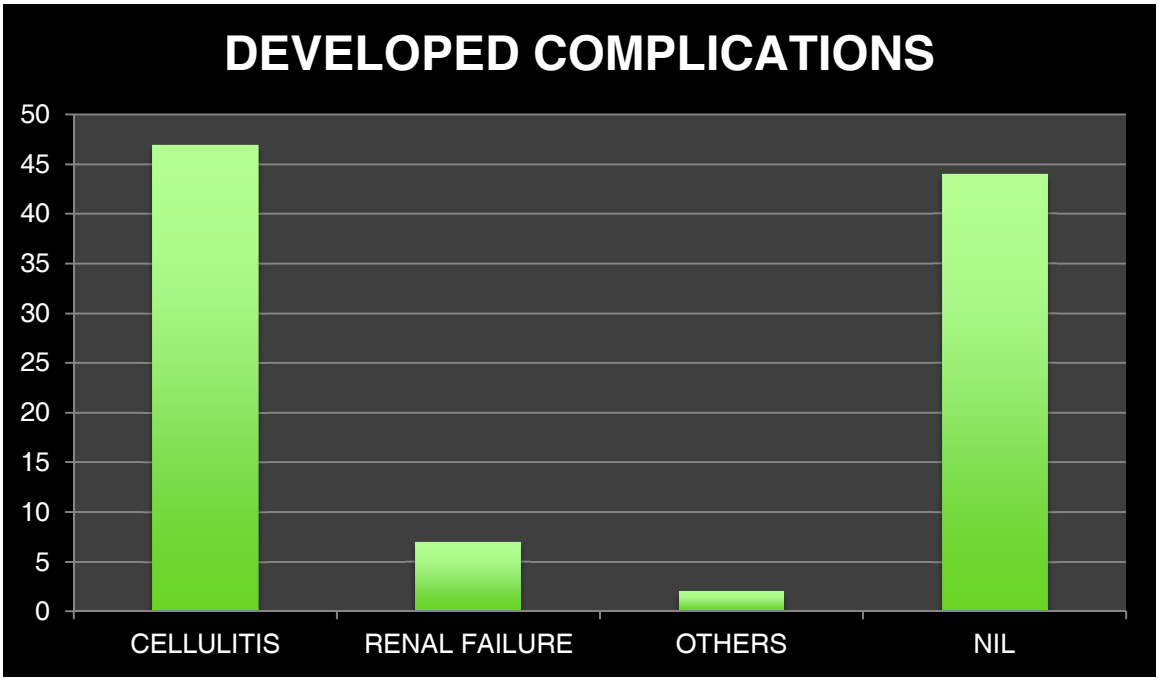



8% of the snake bite cases presented with bleeding manifestation.

**Table : 2.8 DEVELOPED COMPLICATIONS AT PRESENTATION:**

| DEVELOPED COMPLICATIONS | NO. OF PEOPLE |
|---|---|
| CELLULITIS | 47 |
| RENAL FAILURE | 7 |
| OTHERS | 2 |
| NIL | 44 |

**Chart : 2.8 DEVELOPED COMPLICATIONS AT PRESENTATION**

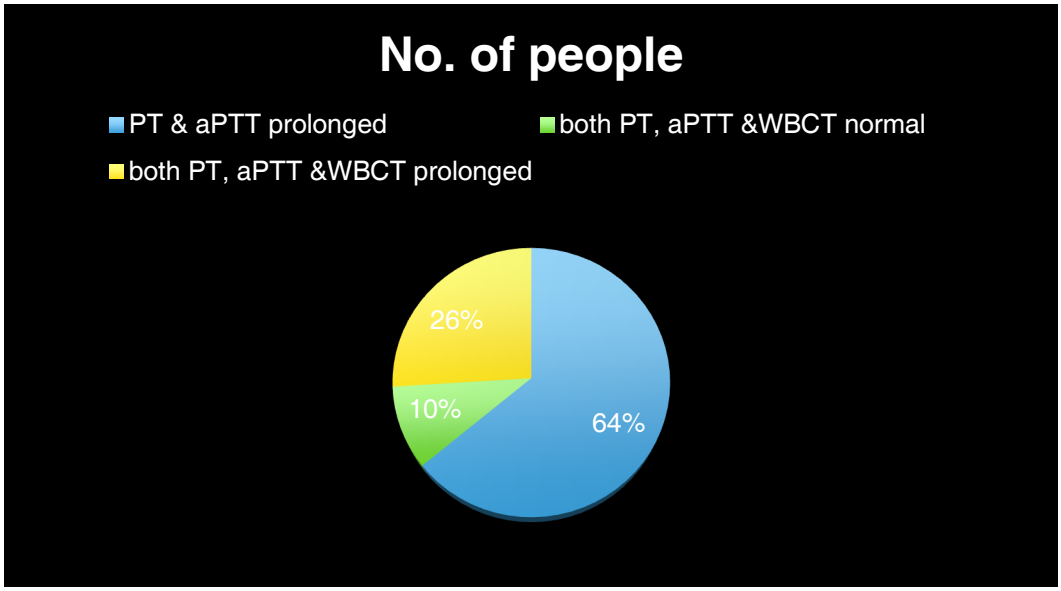



At presentation 47% of cases had cellulitis, 7 % had renal failure and 2% had other complications.

**Table : 2.9 COMPARISON BETWEEN WBCT AND PT &aPTT AT PRESENTATION:**

| AS COMPARED TO WBCT | NO. OF PEOPLE |
|---|---|
| PT AND aPTT along PROLONGED | 64 |
| BOTH NORMAL | 10 |
| BOTH PROLONGED | 26 |

**Chart : 2.9 COMPARISON BETWEEN WBCT AND PT &aPTT AT PRESENTATION**



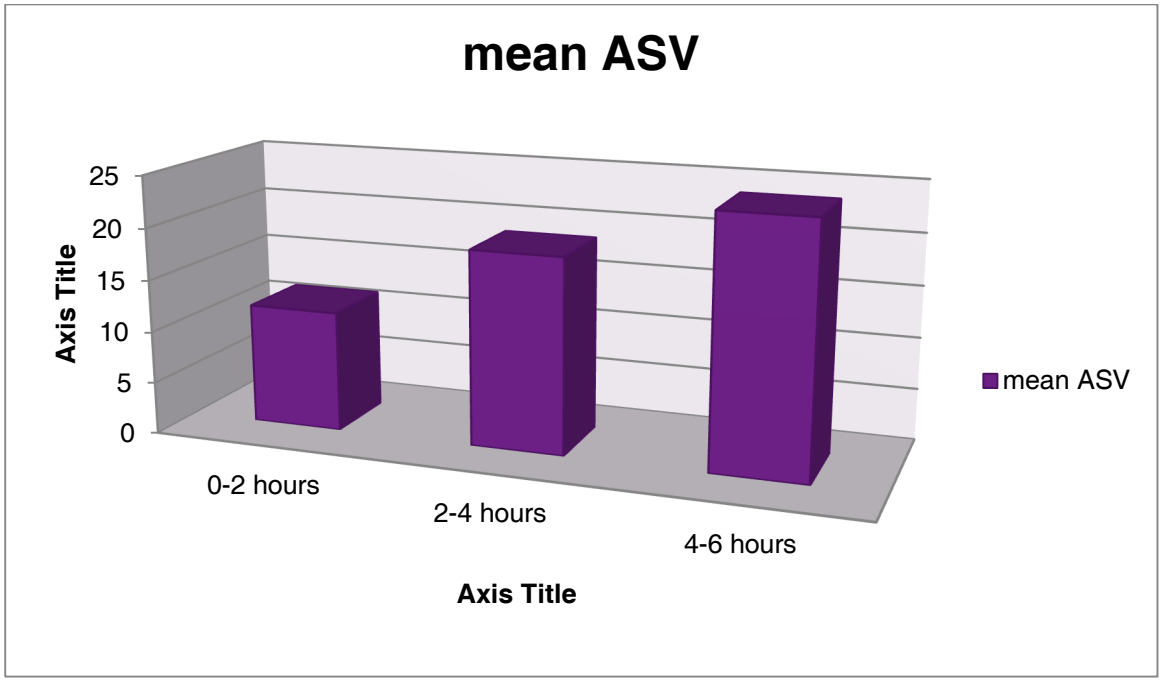

**Management-**

Patients found to have increased 20 minute WBCT were treated with standard dose of ASV 10 vials. Hematotoxic patients were monitored clinically with 20 minute WBCT was repeated after 6 hours. And those with increased 20 minute WBCT value given additional dose of 10 vials of ASV. A maximum of 30 vials of ASV was given, 17 patients received 30 vials of ASV.

**Table : 3.0 ASV REQUIREMENT VS TIME OF PRESENTATION**

| No. of people received ASV | 0 vials | 10 vials | 20 vials | 30 vials | Mean ASV vials re-ceived |
|---|---|---|---|---|---|
| 0-2 hours | 1 | 24 | 6 | 0 | 11.6 |
| 2-4 hours | 0 | 7 | 32 | 2 | 18.78 |
| 4-6 hours | 2 | 0 | 11 | 15 | 23.93 |

**Chart : 3.0 ASV REQUIREMENT VS TIME OF PRESENTATION**



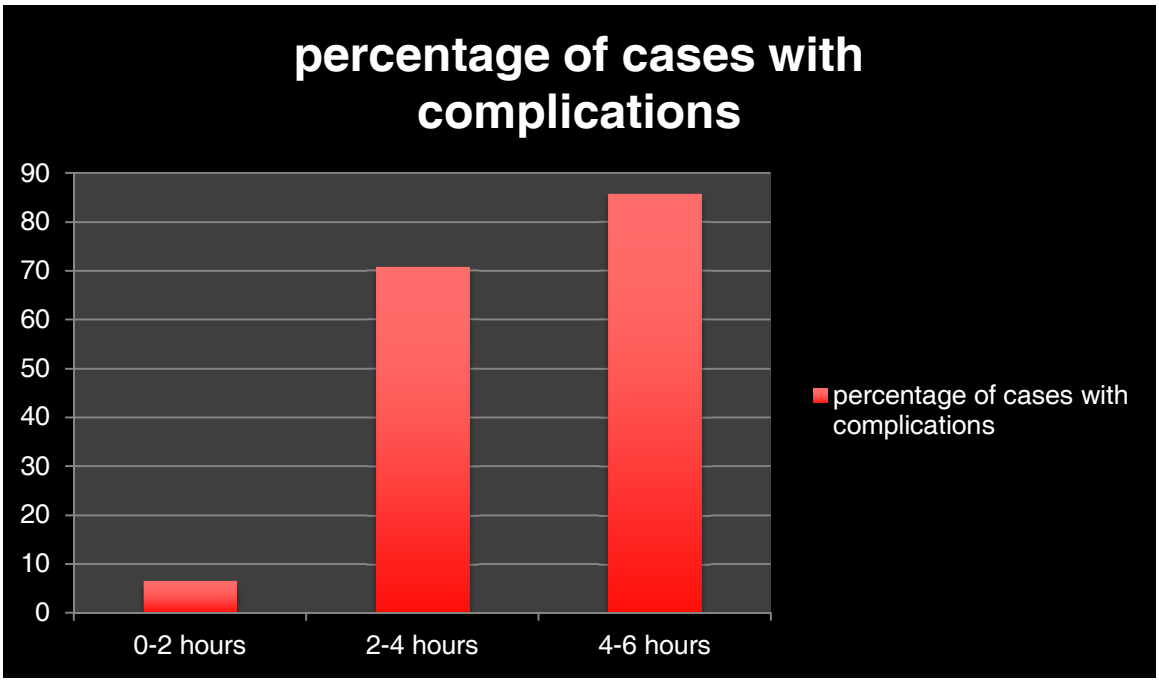

ASV received by patient increase with late presentation , within 2 hours of bite mean ASV used is 19% and that of 4-6 hours is 24%.

**Final outcome**

**Table : 3.1 DEVELOPED COMPLICATION DURING THE COURSE OF TREATMENT**

| Final outcome | complication | No complication | Percentage of cases with complications |
|---|---|---|---|
| 0-2 hours | 2 | 29 | 6.5% |
| 2-4 hours | 29 | 12 | 70.7% |
| 4-6 hours | 24 | 4 | 85.7% |

**Table : 3.1 DEVELOPED COMPLICATION DURING THE COURSE OF TREATMENT**

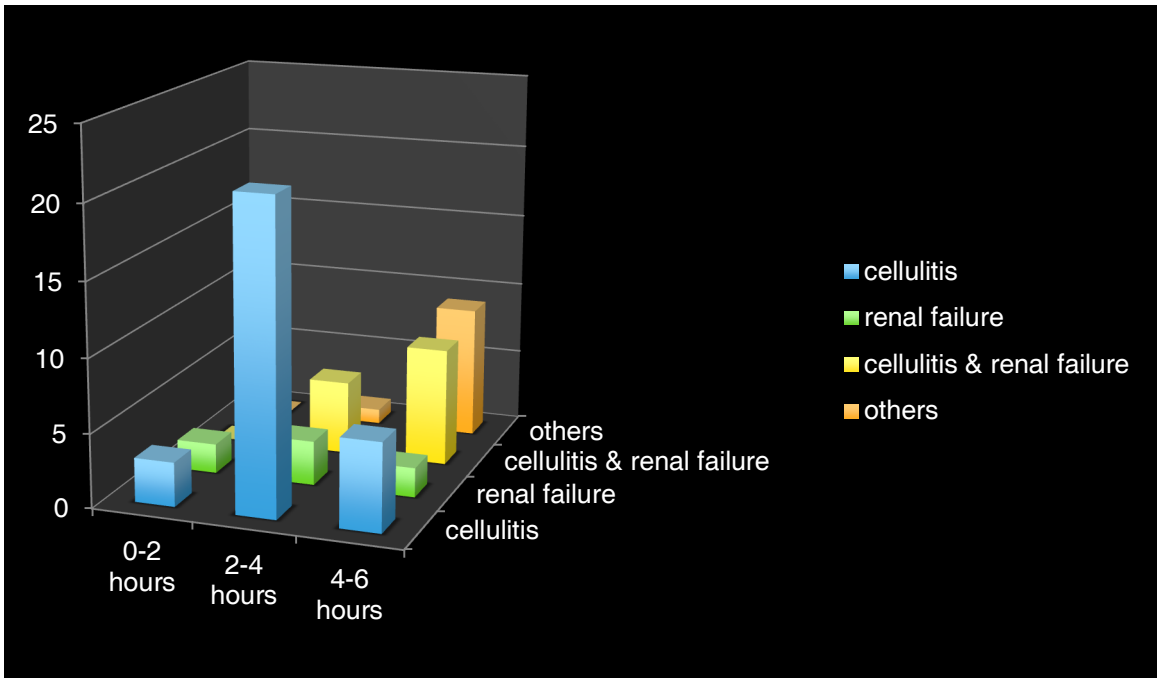



As the time from bite to treatment get delayed complications also develops more, as in the case of 4-6 hours , where 86% develop complications.

**Table : 3.2 Complications in various hours of presentation**

| | cellulitis | Renal failure | Cellulitis and renal failure | Others |
|---|---|---|---|---|
| 0-2 hours | 3 | 2 | 0 | 0 |
| 2-4 hours | 21 | 3 | 5 | 1 |
| 4-6 hours | 6 | 2 | 8 | 9 |

**Chart : 3.2 Complications in various hours of presentation**

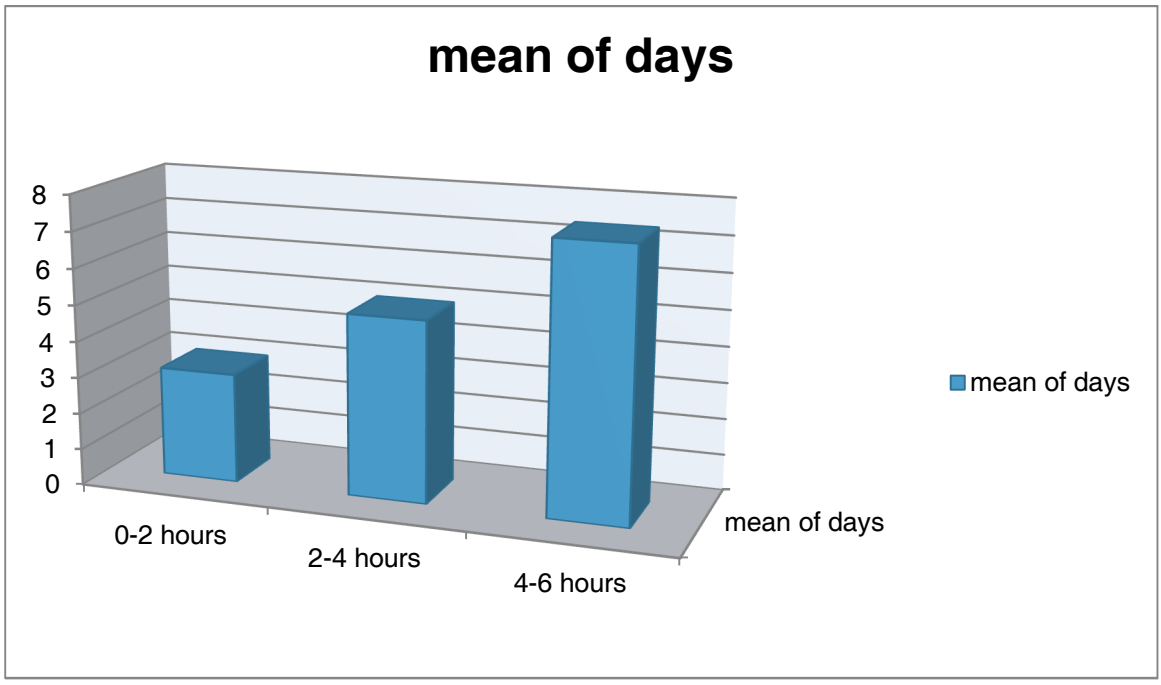



Cellulitis and renal failure are the most common complications.

**Table : 3.3 Duration of Hospital stay**

| | Number of days | Mean |
|---|---|---|
| 0-2 hours | 94 | 3.03 |
| 2-4 hours | 205 | 5 |
| 4-6 hours | 208 | 7.4 |

**Chart : 3.3 Duration of Hospital stay**

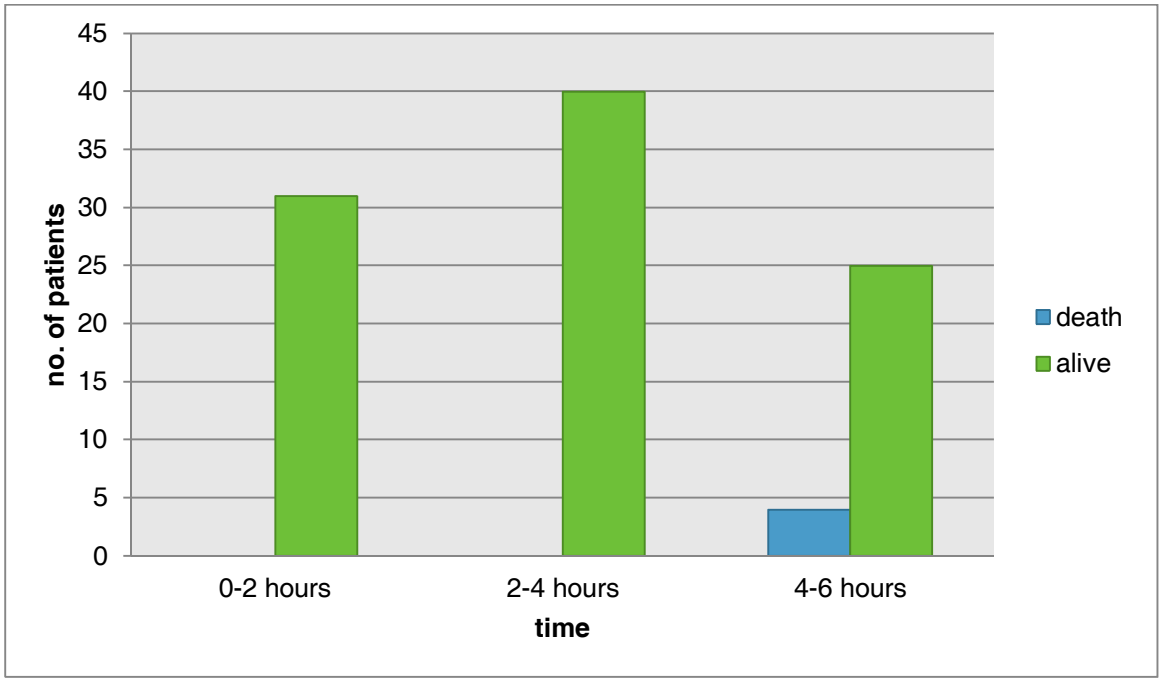



On an average case who presented between 4-6 hours had 7.4 days of hospital stay , as compare to 0-2 hours which had 3 days.

**Table : 3.4 Mortality among the various groups**

| Final Out come | Death | Alive |
|---|---|---|
| 0-2 hours | 0 | 31 |
| 2-4 hours | 0 | 41 |
| 4-6 hours | 4 | 24 |

**Chart: 3.4 Mortality among the various groups**




4 of the cases in snake bite within 4-6 hours died.

**Table :3.5 statistic correlation between PT, aPTT and WBCT in the study groups**

| TIME | PT & aPTT at presentation | WBCT at presentation |
|---|---|---|
| 0-2 HOURS | 26 | 0 |
| 2-4 HOURS | 37 | 8 |
| 4-6 HOURS | 26 | 18 |
| P VALUE – 0.048 | | |
| Pearson P test | | |
| SIGNIFICANT | | |

There is a statistical difference between PT & aPTT over Whole Blood Clotting Time with a confidence interval of 95%.

**Table : 3.6 statistic relation between the study groups with the complications**

| | **FINAL OUTCOME** | |
|---|---|---|
| **TIME** | **Complications** | **No complications** |
| 0-2 HOURS | 5 | 26 |
| 2-4 HOURS | 30 | 11 |
| 4-6 HOURS | 25 | 3 |
| P VALUE - 0.27 | | |
| NOT SIGNIFICANT | | |
| T TEST | | |

Though there was a good number of person who didn't developed complications(who received ASV early) as compared to person who received late ASV. Statistically it was not significant, this could be because of small sample size.

**Table: 3.7 statistic correlation between the study groups and number of ASV administered**

| TIME | NO. OF PEOPLE | NO. OF ASV |
|---|---|---|
| 0-2 HOURS | 31 | 360 |
| 2-4 HOURS | 41 | 750 |
| 4-6 HOURS | 28 | 700 |
| P VALUE= 0.021 | | |
| SIGNIFICANT | | |
| T TEST | | |

There is statistically significant difference between the requirement of ASV in person who received early ASV as compared to late ASV administration.

**Table : 3.8 statistic correlation between the study groups with the final outcome**

| TIME | DEATH | ALIVE |
|---|---|---|
| 0-2 HOURS | 0 | 31 |
| 2-4 HOURS | 0 | 40 |
| 4-6 HOURS | 4 | 25 |
| P VALUE= 0.012 | | |
| SIGNIFICANT | | |
| T TEST | | |

There is statistically significant difference between the final outcome of person who received early ASV as compare to late ASV administration.

# DISCUSSION

In the present study, maximum incidence of snake bite was found in the age of 26-35 years comprising of 56%.80% of the snake bite occurred in males attributed mainly to their outdoor activity compared to females.3% of the snake bites were dry bite, haematotoxic (Viper bite), constituting to 97% of which 5% developed neurotoxicity (respiratory failure). Complications of hematotoxic bite were that 30% developed cellulitis, 7% developed renal failure, 13% developed both cellulitis and renal failure and the rest 10% developed other complications, which are more common complications of Russell"s Viper as seen in South India population[52] . 26 % was identified as Russell's Viper, where as 74% could not be identified as majority the bites occur in the dark 73%. Bleeding manifestation in the form of bleeding from bite site, mucosal bleed and gum bleed were seen in 8% of the study population. Thus hematotoxic snakebite it is now well recognized that such a strict categorization is not valid as each species can result in any kind of manifestations.

31 of the snake bite presented within 2 hours of bite, 41 within 2-4 hours and 28 within 4-6 hours, the delay in presentation was due to delay referral , delay in transportation and lack of awareness . 30% of patients received ASV within 2 hours of snake bite; 40% of patients within 2 to 4 hours, 27 % of patients in 4 to 6 hours, about 3 % of patient did not required ASV, thus indicating Dry bite . 31 patients received 10 vials of ASV .48 patients received 20 vials of ASV.18 patients received 30 vials of ASV. The mean ASV received by

patient who presented at 0-2 hours of bite was11.6 vials, 2-4 hours was 18.78 vials and 4-6 hours was 23.92 vials. Complications developed in patient presenting within 0-2 hours was 6.5%, within 2-4 hours was 70.7% and within 4-6 hours was 85.7% . The mean duration of stay in hospital among patient who presented within 0-2 hours was 3.03 days, within 2-4 hours was 5 days and that of 4-6 hours was 7.42 days. Thus indicating that early initiation of ASV, decreases the amount of ASV requirement , decreases the complications and decreases the stay in hospital. It is also cost effective in treatment.

Mortality rate in the study was 4 out of 100 which was in comparison with the national data 4.5 – 5 out of 100 deaths annually[51]. 1 was a female and others 3 were male , the mean age was 42.75 years , all of the presented at 6 hours of bite with bleeding manifestation. 3 of them had renal failure and had to undergo dialysis. 3 had pre existing co morbidities. Mean ASV used was 30 vials and mean duration of stay in hospital was 12.5 days.

64 % of study population had PT and aPTT alone prolongation, where majority of them presented with 3 hours of snake bite, i.e 54 out of 64. 26 % of study population had both PT & aPTT and WBCT prolongation , and 10 % had both the test as normal. Thus screening of patients with Prothrombin Time will help to detect coagulopathy earlier so that antisnake venom (ASV) can be administered earlier and further complications of coagulopathy can be prevented as well as number of vials of ASV given can be reduced in number.

# CONCLUSIONS

- Snake bite is a major health hazard in a tropical country like India being significantly associated with morbidity and mortality.
- Incidence of snake bite is more common in males compared to females due to their more outdoor activity.
- Even if there is no evidence of envenomation, when they arrive patients should be admitted for observation, ideally for 24 hours. Every hourly monitoring of hematotoxicity, level of consciousness, ptosis, pulse rate and rhythm, blood pressure, respiratory rate, extent of local swelling should be recorded.
- Haematological abnormalities are very common in snake envenomation especially in viperidae bites.
- Manifestations like bite site bleeding, gum bleeding, hematuria, injection site bleeding are clinical indicators of hematotoxicity which can be prevented by earlier interventation with anti-snake venom (ASV).
- Many guidelines described an abnormal 20 minute whole blood clotting test as a marker of coagulation abnormality.However Prothrombin Time will be prolonged earlier compared to Whole Blood Clotting Test and before clinical manifestations of hematotoxicity due to snake envenomation and is relatively more sensitive, but clotting time will be significantly prolonged in severe deficiencies of the various coagulation factors.

- So Prothrombin Time is a very useful blood investigation in making early diagnosis of Coagulopathy when managing hematotoxic snake bite cases compared to Whole Blood Clotting Test.

# LIMITATIONS

- **Small number of patients-**

  Numbers of patients studied in this study are 100 only. Hence no major conclusions can be drawn.

- **Delay in arrival-**

  Prothrombin time is better and earlier predictor of toxicity compared to Whole Blood Clotting Test, however if patients present late to the hospital both PT and WBCT found to be prolonged. In this case bedside done WBCT gives earlier indication of impaired coagulation compared to PT which is done in laboratory.

- **Cost-**

  Since the test has to be repeated at regular intervals to diagnose coagulopathy earlier and it involves use of reagents and cost of the evaluation increases compared to WBCT.

- **Laboratory support-**

  Measurement of prothrombin time needs other reagents and centrifugation, which may not be available in peripheral small health centres in these settings bedside WBCT is more helpful compared to prothrombin time.

- **Simplicity of Whole Blood Clotting Test-**

  Measurement of prothrombin time requires skilled laboratory person while assessment of bedside WBCT is a simple test which do not require skilled laboratory person.

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# PERFOMA

Name : Age :

Sex : Place :

**Date of admission :**

I) Date and time of bite:

II) Type of snake:

**Presenting complaints :**

1. Bleeding from bite site (+/-)
2. Gum bleeding(+/-)
3. Hematuria(+/-)
4. Hematemesis(+/-)
5. Epistaxis(+/-)
6. Conjunctival hemorrhage(+/-)
7. Petechiae(+/-)
8. Purpura(+/-)
9. Other complaints

**General examination:**

| | | | | | |
|---|---|---|---|---|---|
| Temperature | - | B.P. | - | Pulse | - |
| Respiratory rate | - | Pallor | - | Icterus | - |
| Clubbing | - | Cyanosis | - | Edema | - |

Tender lymphadenopathy -

**Local examination**

Fang mark (+/-)

Cellulitis (+/-)

**Systemic examination :**

Respiratory system -

Cardiovascular system -

Per–abdomen -

Central nervous system -

| **Sample** | **Time** | **Prothrombin Time (PT)** | **aPTT** | **Whole blood clotting time** |
|---|---|---|---|---|
| 1 | | | | |
| 2 | | | | |

Time of Snake Bite →

Time of First Prolonged PT →

Time of First Prolonged CT →

Whether PT is prolonged before CT or not → Yes/No

Duration of time gap between First PT & →

First CT Prolongation

**HOSPITAL COURSE:**

DATE / TIME:

ASV DOSE REQUIRED-

ADVERSE REACTION TO ASV- YES/NO

TIME TO NORMALISATION OF CLOTTING TIME:

COMPLICATIONS-

RECURRENCE OF COAGULOPATHY : YES / NO

# ஒப்புதல் படிவம்

பெயர் :

வயது :

பாலினம் :

முகவரி :

கோவை அரசு மருத்துவக் கல்லூரி மருத்துவமனையில் மரு. மசிசிலி ஜூமு தலைமையில் நடைபெறும் இந்த ஆய்வில் எனது முழுஉடல் மற்றும் இரத்தப் பரிசோதனை செய்து கொள்ள முழு மனதுடன் சம்மதிக்கிறேன். என்னைப் பற்றிய விவரங்களை பாதுகாப்புடன் இந்த ஆய்வில் வெளியிட ஆட்சேபணை இல்லை என்று தெரிவித்துக் கொள்கிறேன். நான் எந்த நேரத்திலும் ஆய்வில் இருந்து விலக்கிக் கொள்ளும் உரிமை உண்டு என்று அறிவேன்.

இடம் கையொப்பம்/கைரேகை

தேதி

# STATEMENT OF CONSENT

I, _____, do hereby volunteer and consent to participate in this study being conducted by Dr. MHASISIELIE ZUMU ,I have read and understood the consent form (or) it has been read and explained to me thoroughly. I am fully aware of the study details as well as aware that I may ask questions to him at any time.

Signature / Left Thumb Impression of the patient

Station: Coimbatore

Date:

Signature / Left Thumb Impression and Name of the witness

Station: Coimbatore

Date:

# MASTER CHART

| Name | age | sex | Time of bite | time of presentation in hours | place of bite | type of snake | bleeding manifestation | Pulse Rate | Blood Pressure in mm Hg | BITE MARK | cellulitis at presentation | whole blood clotting time in Minutes | complication | comorbidities | aPTT | PT | ASV | outcome | hospital stay in days |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Krishnasamy | 40 | M | D | 2 | OUTDOOR | RUSSEL VIPER | no | 90 | 120/90 | YES | NO | <20 | nil | SHTN | prolong | prolong | 10 | recovered | 3 |
| Murugan | 34 | M | N | 4 | OUTDOOR | NOT KNOWN | no | 80 | 130/90 | YES | NO | >20 | renal failure, respiratory failure | nil | prolong | prolong | 20 | recovered | 6 |
| Gurusamy | 41 | M | N | 4 | OUTDOOR | NOT KNOWN | no | 92 | 120/80 | YES | NO | <20 | cellulitis | SHTN | prolong | prolong | 20 | recovered | 5 |
| Ramakrishnan | 37 | M | D | 5 | OUTDOOR | RUSSELL VIPER | no | 94 | 110/80 | YES | yes | >20 | cellulitis,renal failure | nil | prolong | prolong | 30 | recovered | 8 |
| MuthusamY | 28 | M | N | 1.5 | OUTDOOR | NOT KNOWN | no | 96 | 110/80 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 3 |
| Raja | 26 | M | N | 5 | OUTDOOR | NOT KNOWN | no | 97 | 100/70 | YES | YES | >20 | cellulitis | nil | prolong | prolong | 20 | recovered | 5 |
| Aruchamy | 43 | M | N | 1.5 | OUTDOOR | NOT KNOWN | no | 87 | 120/80 | YES | NO | <20 | nil | SHTN | prolong | prolong | 10 | recovered | 3 |
| Priya | 31 | F | N | 1 | OUTDOOR | NOT KNOWN | no | 85 | 110/70 | YES | NO | <20 | nil | nil | normal | normal | 0 | recovered | 2 |
| Vignesh | 32 | M | N | 2.5 | HOME | RUSSELL VIPER | no | 96 | 120/80 | YES | NO | <20 | nil | nil | prolong | prolong | 20 | recovered | 4 |
| Gowri | 27 | F | N | 5.5 | OUTDOOR | NOT KNOWN | no | 76 | 110/70 | YES | NO | <20 | renal failure | nil | prolong | prolong | 20 | recovered | 5 |
| Velusamy | 43 | M | N | 6 | OUTDOOR | NOT KNOWN | yes | 82 | 140/90 | YES | YES | >20 | sepsis,ARDS | SHTN | prolong | prolong | 30 | death | 13 |
| Satish | 24 | M | D | 2.5 | OUTDOOR | NOT KNOWN | no | 81 | 130/90 | YES | NO | <20 | cellulitis, renal failure | nil | prolong | prolong | 20 | recovered | 6 |
| Mari | 29 | F | N | 1 | OUTDOOR | NOT KNOWN | no | 83 | 120/80 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 3 |
| Harshini | 31 | F | D | 2.5 | WORK | RUSSEL VIPER | no | 84 | 120/80 | YES | NO | <20 | cellulitis | nil | prolong | prolong | 10 | recovered | 4 |
| Mirdhula | 36 | F | N | 1.5 | OUTDOOR | NOT KNOWN | no | 91 | 110/80 | YES | NO | <20 | renal failure | nil | prolong | prolong | 20 | recovered | 4 |
| Preethi | 37 | F | N | 3 | OUTDOOR | NOT KNOWN | no | 95 | 110/70 | YES | NO | <20 | cellulitis | SHTN | prolong | prolong | 20 | recovered | 4 |
| Divya | 44 | F | N | 6 | OUTDOOR | NOT KNOWN | yes | 73 | 150/90 | NO | YES | >20 | renal failure, DIC | SHTN, DM | prolong | prolong | 30 | death | 15 |
| Barathi | 28 | M | N | 1.5 | OUTDOOR | RUSSELL VIPER | no | 75 | 100/80 | YES | NO | <20 | nil | nil | normal | normal | 10 | recovered | 3 |
| Sadhasivam | 27 | M | N | 4.5 | OUTDOOR | NOT KNOWN | no | 76 | 130/80 | YES | NO | <20 | cellulitis, respiratory failure | nil | prolong | prolong | 30 | recovered | 8 |
| Harrini | 37 | F | N | 2 | OUTDOOR | NOT KNOWN | no | 81 | 110/70 | YES | NO | <20 | nil | DM | normal | normal | 10 | recovered | 2 |
| Suresh | 21 | M | N | 2 | OUTDOOR | NOT KNOWN | no | 83 | 130/80 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 3 |
| Abishek | 26 | M | D | 2.5 | OUTDOOR | RUSSEL VIPER | no | 84 | 120/70 | YES | NO | <20 | cellulitis | nil | prolong | prolong | 20 | recovered | 5 |
| Akshaya | 38 | F | D | 1.5 | OUTDOOR | RUSSELL VIPER | no | 94 | 110/80 | YES | NO | <20 | nil | old CVA | prolong | prolong | 10 | recovered | 2 |
| Arun | 23 | M | N | 3 | OUTDOOR | NOT KNOWN | no | 86 | 130/90 | YES | yes | <20 | cellulitis | nil | prolong | prolong | 20 | recovered | 5 |
| Karthik | 45 | M | N | 3 | OUTDOOR | NOT KNOWN | no | 84 | 150/90 | YES | NO | <20 | nil | DM | normal | normal | 10 | recovered | 3 |
| Bala | 34 | M | N | 3 | OUTDOOR | NOT KNOWN | no | 68 | 120/80 | YES | NO | <20 | cellulitis | nil | prolong | prolong | 20 | recovered | 5 |
| Ganesh | 36 | M | N | 1.5 | OUTDOOR | NOT KNOWN | no | 81 | 130/80 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 4 |
| Arvind | 31 | M | N | 5 | OUTDOOR | NOT KNOWN | no | 76 | 100/70 | YES | NO | <20 | nil | nil | normal | normal | 0 | recovered | 2 |
| Ramesh | 23 | M | N | 4 | OUTDOOR | NOT KNOWN | no | 64 | 120/80 | YES | NO | >20 | cellulitis | nil | prolong | prolong | 20 | recovered | 7 |
| Krishna | 29 | F | N | 5 | OUTDOOR | NOT KNOWN | no | 55 | 110/80 | YES | NO | <20 | cellulitis,  renal failure | hypothyroid | prolong | prolong | 20 | recovered | 6 |
| Karupusamy | 31 | M | N | 2.5 | OUTDOOR | NOT KNOWN | no | 75 | 130/90 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 4 |
| Jeyabalaji | 37 | M | D | 3 | OUTDOOR | RUSSEL VIPER | no | 96 | 140/90 | YES | NO | >20 | cellulitis,renal failure | nil | prolong | prolong | 20 | recovered | 7 |
| Vinothkumar | 30 | M | D | 1.5 | OUTDOOR | RUSSELL VIPER | no | 85 | 150/80 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 2 |
| Denish | 24 | M | N | 3 | HOME | NOT KNOWN | no | 75 | 140/90 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 3 |
| Vinkethachalam | 31 | M | N | 5 | OUTDOOR | NOT KNOWN | no | 65 | 140/80 | YES | yes | >20 | cellulitis, sepsis | nil | prolong | prolong | 30 | recovered | 8 |
| Peter | 23 | M | N | 3 | OUTDOOR | NOT KNOWN | no | 75 | 130/80 | YES | NO | <20 | nil | nil | prolong | prolong | 20 | recovered | 4 |
| Balaji | 38 | M | N | 6 | OUTDOOR | NOT KNOWN | yes | 94 | 100/80 | YES | yes | >20 | cellulitis, respiratory failure | nil | prolong | prolong | 30 | recovered | 9 |
| Kavita | 35 | F | D | 1 | OUTDOOR | RUSSELL VIPER | no | 84 | 110/70 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 3 |
| Ragavendra | 33 | M | N | 5 | OUTDOOR | NOT KNOWN | no | 86 | 120/80 | YES | NO | <20 | cellulitis, renal failure | nil | prolong | prolong | 20 | recovered | 6 |
| Gurumoorthy | 41 | M | N | 3 | OUTDOOR | NOT KNOWN | no | 82 | 110/70 | YES | NO | <20 | cellulitis | DM | prolong | prolong | 20 | recovered | 7 |
| Vishnu | 22 | F | N | 6 | OUTDOOR | NOT KNOWN | yes | 110 | 90/70 | YES | NO | >20 | cellulitis,respiratory failure | nil | prolong | prolong | 30 | recovered | 8 |
| Elango | 28 | M | N | 5 | OUTDOOR | NOT KNOWN | no | 100 | 90/70 | YES | NO | >20 | cellulitis | nil | prolong | prolong | 20 | recovered | 6 |
| Nithin | 34 | M | N | 2.5 | OUTDOOR | RUSSEL VIPER | no | 86 | 110/70 | YES | YES | <20 | nil | nil | prolong | prolong | 20 | recovered | 4 |

| Name | age | sex | Time of bite | time of presentation in hours | place of bite | type of snake | bleeding manifestation | Pulse Rate | Blood Pressure in mm Hg | BITE MARK | cellulitis at presentation | whole blood clotting time in Minutes | complication | comorbidities | aPTT | PT | ASV | outcome | hospital stay in days |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Shaktivel | 29 | M | N | 5 | OUTDOOR | NOT KNOWN | no | 84 | 100/70 | YES | NO | >20 | cellulitis, sepsis , renal failure | nil | prolong | prolong | 30 | recovered | 9 |
| Mahesh kumar | 25 | M | D | 1.5 | OUTDOOR | NOT KNOWN | no | 78 | 120/80 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 3 |
| Rajgokul | 22 | M | N | 2 | OUTDOOR | NOT KNOWN | no | 67 | 110/80 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 2 |
| Bhuvaneshwari | 27 | F | D | 5 | OUTDOOR | NOT KNOWN | no | 91 | 90/70 | YES | NO | >20 | cellulitis, sepsis | nil | prolong | prolong | 20 | recovered | 6 |
| Vishuram | 40 | M | N | 2.5 | OUTDOOR | NOT KNOWN | no | 88 | 110/80 | YES | NO | <20 | cellulitis | DM | prolong | prolong | 20 | recovered | 5 |
| Deepika | 18 | F | D | 1.5 | OUTDOOR | RUSSELL VIPER | no | 83 | 100/70 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 2 |
| Prashant | 42 | M | N | 2.5 | OUTDOOR | NOT KNOWN | no | 84 | 130/90 | YES | NO | <20 | renal failure | nil | prolong | prolong | 20 | recovered | 5 |
| Durga | 20 | F | N | 3 | OUTDOOR | NOT KNOWN | no | 86 | 110/70 | YES | NO | >20 | nil | nil | prolong | prolong | 20 | recovered | 4 |
| Gaurave | 42 | M | N | 5 | OUTDOOR | NOT KNOWN | yes | 94 | 90/60 | YES | NO | >20 | cellulitis, renal failure | DM | prolong | prolong | 30 | recovered | 10 |
| Dinu | 17 | F | N | 6 | HOME | NOT KNOWN | no | 82 | 100/70 | YES | NO | <20 | nil | nil | prolong | prolong | 20 | recovered | 4 |
| Shivakumar | 34 | M | D | 3 | OUTDOOR | RUSSEL VIPER | no | 76 | 120/80 | YES | YES | <20 | cellulitis | nil | prolong | prolong | 20 | recovered | 4 |
| Jaganath | 38 | M | N | 4 | OUTDOOR | NOT KNOWN | no | 84 | 110/80 | YES | NO | >20 | renal failure | DM | prolong | prolong | 20 | recovered | 6 |
| Vigneshawaran | 26 | M | D | 3 | OUTDOOR | NOT KNOWN | no | 86 | 100/80 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 2 |
| Nekhil | 34 | M | N | 1 | OUTDOOR | NOT KNOWN | no | 85 | 120/80 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 3 |
| Ganesh moorthy | 36 | M | N | 3 | HOME | NOT KNOWN | no | 75 | 100/80 | YES | NO | <20 | cellulitis | nil | prolong | prolong | 20 | recovered | 6 |
| Surya | 27 | M | N | 5 | OUTDOOR | NOT KNOWN | no | 94 | 100/80 | YES | NO | >20 | cellulitis, renal failure, sepsis | nil | prolong | prolong | 30 | recovered | 9 |
| Karthikeyan | 35 | M | D | 2.5 | OUTDOOR | RUSSELL VIPER | no | 76 | 110/70 | YES | YES | <20 | cellulitis | nil | prolong | prolong | 20 | recovered | 5 |
| Aartha | 32 | F | N | 5 | OUTDOOR | NOT KNOWN | no | 96 | 110/80 | YES | NO | <20 | nil | nil | normal | normal | 0 | recovered | 2 |
| Marimithu | 30 | M | D | 4 | OUTDOOR | NOT KNOWN | no | 82 | 100/70 | YES | NO | <20 | cellulitis | nil | prolong | prolong | 20 | recovered | 5 |
| Vijay | 34 | M | D | 2 | OUTDOOR | RUSSEL VIPER | no | 84 | 120/80 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 3 |
| Rajprabu | 44 | M | N | 1.5 | OUTDOOR | NOT KNOWN | no | 76 | 130/80 | YES | NO | <20 | cellulitis | DM,SHTN | prolong | prolong | 20 | recovered | 5 |
| Ravikumar | 29 | M | D | 6 | OUTDOOR | RUSSELL VIPER | yes | 73 | 80/60 | YES | yes | >20 | cellulitis | nil | prolong | prolong | 30 | recovered | 9 |
| Puvi | 41 | M | D | 3 | OUTDOOR | RUSSEL VIPER | no | 79 | 130/90 | YES | NO | <20 | cellulitis, renal failure | SHTN | prolong | prolong | 20 | recovered | 6 |
| Shakti | 31 | M | N | 2 | OUTDOOR | NOT KNOWN | no | 98 | 150/90 | YES | NO | <20 | cellulitis | nil | normal | normal | 20 | recovered | 5 |
| Ramasamy | 27 | M | N | 5 | OUTDOOR | NOT KNOWN | no | 88 | 130/80 | YES | NO | <20 | cellulitis | nil | prolong | prolong | 20 | recovered | 5 |
| Twushif | 30 | M | N | 3 | OUTDOOR | RUSSELL VIPER | no | 87 | 120/80 | YES | NO | <20 | cellulitis, renal failure | nil | prolong | prolong | 20 | recovered | 6 |
| Mani | 27 | M | N | 1 | OUTDOOR | NOT KNOWN | no | 76 | 110/70 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 2 |
| Mukeshkumar | 33 | M | N | 2.5 | HOME | NOT KNOWN | no | 76 | 110/80 | YES | NO | <20 | cellulitis | nil | prolong | prolong | 20 | recovered | 6 |
| Rahul | 35 | M | N | 5 | OUTDOOR | NOT KNOWN | no | 85 | 100/70 | YES | NO | >20 | cellulitis, renal failure | nil | prolong | prolong | 30 | recovered | 9 |
| Dedana | 28 | F | D | 3 | OUTDOOR | RUSSEL VIPER | no | 72 | 110/80 | YES | NO | >20 | cellulitis | hypothyroid | prolong | prolong | 30 | recovered | 8 |
| Vasanthan | 32 | M | N | 1.5 | OUTDOOR | NOT KNOWN | no | 76 | 130/80 | YES | NO | <20 | nil | nil | prolong | prolong | 20 | recovered | 4 |
| Senthil | 37 | M | D | 4 | OUTDOOR | RUSSELL VIPER | no | 73 | 150/90 | YES | YES | >20 | cellulitis | SHTN | prolong | prolong | 20 | recovered | 6 |
| Brinda | 35 | F | N | 3 | HOME | NOT KNOWN | no | 64 | 110/80 | YES | NO | <20 | renal failure | nil | normal | normal | 10 | recovered | 5 |
| Mutikumar | 38 | M | N | 2.5 | OUTDOOR | NOT KNOWN | no | 68 | 120/80 | YES | NO | <20 | nil | Seizure | prolong | prolong | 10 | recovered | 2 |
| Madhavan | 29 | M | N | 1.5 | OUTDOOR | NOT KNOWN | no | 94 | 130/80 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 3 |
| Seelvamani | 25 | M | N | 2.5 | OUTDOOR | RUSSEL VIPER | no | 84 | 120/80 | YES | NO | <20 | cellulitis, renal failure | nil | prolong | prolong | 20 | recovered | 5 |
| Bhoobalan | 21 | M | N | 5 | OUTDOOR | NOT KNOWN | no | 76 | 110/80 | YES | NO | >20 | cellulitis | nil | prolong | prolong | 20 | recovered | 6 |
| Nagaraj | 23 | M | N | 6 | OUTDOOR | NOT KNOWN | no | 69 | 100/70 | YES | NO | <20 | cellulitis | nil | prolong | prolong | 20 | recovered | 4 |
| Deepath | 29 | M | N | 2 | OUTDOOR | NOT KNOWN | no | 76 | 110/80 | YES | YES | <20 | nil | nil | prolong | prolong | 20 | recovered | 4 |
| Ramprakash | 39 | M | D | 6 | OUTDOOR | RUSSEL VIPER | yes | 95 | 100/70 | YES | yes | >20 | renal failure, sepsis, cellulitis | nil | prolong | prolong | 30 | death | 12 |
| Shiva | 20 | M | N | 3 | OUTDOOR | NOT KNOWN | no | 96 | 140/90 | YES | NO | <20 | cellulitis | nil | prolong | prolong | 20 | recovered | 5 |
| Rajeshwaran | 17 | M | N | 1.5 | OUTDOOR | NOT KNOWN | no | 85 | 130/90 | YES | NO | <20 | renal failure | Seizure | prolong | prolong | 10 | recovered | 4 |
| Manikandan | 19 | M | N | 5 | OUTDOOR | NOT KNOWN | no | 98 | 120/80 | YES | yes | >20 | cellulitis, renal failure | nil | prolong | prolong | 30 | recovered | 8 |
| Ibrahim | 33 | M | N | 2 | HOME | NOT KNOWN | no | 97 | 130/80 | YES | NO | <20 | cellulitis | nil | prolong | prolong | 20 | recovered | 4 |
| Sastha | 31 | M | N | 1 | OUTDOOR | NOT KNOWN | no | 94 | 120/80 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 3 |
| Siddhu | 28 | M | D | 2 | OUTDOOR | RUSSELL VIPER | no | 92 | 130/80 | YES | NO | <20 | nil | nil | normal | normal | 10 | recovered | 2 |

| Name | age | sex | Time of bite | time of presentation in hours | place of bite | type of snake | bleeding manifestation | Pulse Rate | Blood Pressure in mm Hg | BITE MARK | cellulitis at presentation | whole blood clotting time in Minutes | complication | comorbidities | aPTT | PT | ASV | outcome | hospital stay in days |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Vageshwar | 30 | M | D | 3 | OUTDOOR | NOT KNOWN | no | 91 | 120/80 | YES | NO | <20 | cellulitis | nil | prolong | prolong | 20 | recovered | 4 |
| Naveen | 35 | M | D | 1.5 | OUTDOOR | RUSSELL VIPER | no | 82 | 110/80 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 3 |
| Manoj | 25 | M | N | 3 | OUTDOOR | NOT KNOWN | no | 80 | 120/80 | YES | NO | <20 | cellulitis | nil | normal | normal | 20 | recovered | 6 |
| soundarajan | 31 | M | N | 3 | OUTDOOR | NOT KNOWN | no | 93 | 110/80 | YES | NO | <20 | cellulitis | nil | prolong | prolong | 20 | recovered | 5 |
| Suresh kumar | 24 | M | N | 3 | OUTDOOR | NOT KNOWN | no | 91 | 120/80 | YES | NO | <20 | nil | nil | prolong | prolong | 20 | recovered | 3 |
| Ramanan | 27 | M | N | 5 | OUTDOOR | NOT KNOWN | no | 97 | 130/90 | YES | NO | <20 | renal failure | nil | prolong | prolong | 20 | recovered | 6 |
| Fathima | 33 | F | N | 4 | HOME | NOT KNOWN | no | 110 | 100/70 | YES | YES | >20 | cellulitis | hypothyroid | prolong | prolong | 30 | recovered | 9 |
| Venkatesh | 32 | M | N | 2.5 | OUTDOOR | NOT KNOWN | no | 120 | 110/80 | YES | NO | <20 | nil | nil | prolong | prolong | 20 | recovered | 4 |
| Safik | 30 | M | N | 2 | OUTDOOR | NOT KNOWN | no | 97 | 120/80 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 3 |
| Srinivasan | 29 | M | D | 2 | OUTDOOR | RUSSELL VIPER | no | 62 | 120/90 | YES | NO | <20 | nil | nil | prolong | prolong | 10 | recovered | 2 |
| Veerasamy | 45 | M | D | 6 | OUTDOOR | RUSSELL VIPER | yes | 120 | 80/60 | YES | YES | >20 | renal failure, respiratory failure | DM | prolong | prolong | 30 | death | 10 |